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Dear Sir or Madam:

Re: 8(e) CAP-0103; Data Submission

The enclosed document is submitted pursuant to the TSCA Section 8(e) Compliance Audit Program and the CAP Agreement between Rohm and Haas Company and the Environmental Protection Agency. This document does not contain confidential business information.

The following is a summary of the contents of the submission under Unit II.C.3 of the CAP Agreement:

Tested Chemical:	2-Propenamide
CASRN:	79-06-1
Title of Report or Study:	Acrylamide: A Two-Year Drinking Water Chronic Toxicity-Oncogenicity Study in Fischer 344 Rats (Report No. 84RN-1001)
Reportable Effect:	Test substance produced multiple tumor sites and was neurotoxic. (Doses: .01, .1, .5, 2.0 mg/kg/day)

If additional information is required, please contact the undersigned at (215) 592-3139. Thank you.

Sincerely,

Ronald L. Keener

Ronald L. Keener, Ph.D.
Regulatory Affairs Director
Product Integrity Department

RLK:so
Enclosure

DISCLOSURE
9/1/95

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

By

K. A. Johnson, S. J. Gorzinski, K. M. Bodner, and R. A. Campbell

Final Report

21 September 1984

Study sponsored by: American Cyanamid Company, Dow Chemical U.S.A., Nalco Chemical Company, and The Standard Oil Company (Ohio)

Mammalian and Environmental Toxicology Research Laboratory
Health and Environmental Sciences, USA
Dow Chemical, U.S.A.
Midland, Michigan 48640

84RN-1001

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ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

SUMMARY

Groups of male and female Fischer 344 rats (60/sex/dose level) were provided drinking water formulated to deliver either 0 (controls), 0.01, 0.1, 0.5, or 2.0 mg acrylamide/kg body weight/day for 2 years to study the chronic toxic and oncogenic effects of acrylamide. Parameters evaluated were mortality, clinical signs of toxicity, body weights, food consumption, water consumption, clinical chemistry, hematology, urinalysis, gross pathology, organ weights, and histopathology.

Over the course of the study the mean body weight of male rats given 2.0 mg/kg/day was less than control rats. This reached a maximum difference of about 4% less after a year or more on test. Males given 0.5 mg/kg/day and females given 2.0 mg/kg/day had mean body weights about 2% less than their respective control group.

In the last months of study, rats given 2.0 mg/kg/day were noted to have an increased incidence of subcutaneous masses.

There was increased mortality in the group given 2.0 mg/kg/day, especially females. This increase occurred only in the last portion of the study, beginning at about the 21st month. Degeneration of the peripheral nerves, a recognized effect of acrylamide, was noted histopatholcgically in rats given 2.0 mg/kg/day.

Increased incidences of the following tumors were identified as biologically significant in rats given 2.0 mg/kg/day: Females: mammary gland (benign and malignant), central nervous system (malignant), thyroid gland - follicular epithelium (combined benign and malignant), mouth (benign), uterus (malignant), and clitoral gland (benign); Males: scrotal mesothelioma (malignant) and thyroid gland - follicular epithelium (benign).

Male rats given 2.0 mg/kg/day also had increased incidence of central nervous system tumors when compared to historical controls but not when compared to the control group in this study.

Statistically significant increases in the incidence of benign tumors of the pituitary gland in females given 2.0 mg/kg/day and benign tumors of the adrenal medulla in males at the same dose level were considered of questionable biological significance.

The only tumor type significantly increased in male rats given 0.5 mg/kg/day was scrotal mesothelioma. The incidence of benign mammary tumors and clitoral gland tumors (benign and malignant combined) in females at this dose level suggested a treatment-related effect.

Tumor incidence was not significantly elevated in rats given 0.01 or 0.1 mg/kg/day although the incidence of scrotal mesothelioma exceeded concurrent and historical control mean values in male rats given 0.1 mg/kg/day.

In conclusion, under the conditions of this study, acrylamide produces slight peripheral neuropathy and a variety of neoplasms when given to Fischer 344 rats for 2 years.

INTRODUCTION

Acrylamide (CAS No. 79-06-1, 2-propenamide) is a vinyl monomer used to manufacture high molecular weight, water-soluble polymers and copolymers used primarily as flocculating agents and viscosifiers. The major use of polyacrylamide is as a flocculant in water treatment. Polyacrylamide flocculants are also used in mining and ore processing, pulp and paper manufacture, and numerous process industries. As a viscosifier, polyacrylamides are used in oil well drilling and enhanced oil recovery. Polyacrylamides are used for certain food or potable water processing applications under regulations administered by the FDA or EPA.

Acrylamide is of moderate acute toxicity with an LD_{50} of 150-180 mg/kg for rats, guinea pigs, or rabbits (McCollister et al., 1964). It is only slightly irritating to the eye or skin of rabbits. However, repeated exposure produces neurotoxicity in man and a variety of animal species. The nervous system target has been localized to the distal portion of the axon, producing what has been termed a "dying-back" form of neuropathy (reviewed by Spencer and Schaumburg, 1974a and b; LeQuesne, 1980; and Tilson, 1981). The lesion appears to involve both central and peripheral axons although the lesions appear more dramatic in the peripheral nerves. Larger diameter axons are more sensitive than smaller ones and myelinated fibers are affected more than unmyelinated. Recently, reports of morphologic changes in the nerve cell body have challenged the concept of distal axonopathy as being the primary or sole lesion of acrylamide intoxication (Cavanagh, 1982; Sterman, 1982).

In spite of extensive information on the neurotoxic potential of acrylamide, its oncogenic potential had not been assessed at the time this study was initiated. The purpose of the study reported herein was to assess the chronic toxicity and oncogenicity of acrylamide when given to rats for 2 years. Acrylamide was known to be negative in the Ames test for bacterial mutation (Lijinsky and Andrews, 1980) at the time this study was started. Since then several additional studies of mutagenicity or genotoxicity have been reported.

The negative results in the Ames test have been confirmed (Mast et al., 1983; Bull et al., 1983). However, several assays using mammalian cells have produced conflicting results (Mast et al., 1983; Bull et al., 1983; Bull et al., 1984; Miller et al., 1984). Recently acrylamide has been reported as positive in both a mouse skin tumor initiation-promotion study and a mouse lung adenoma induction assay (Bull et al., 1984).

The present study utilized dose levels suggested by the results of 3- and 13-week toxicity studies (Gorzinski et al., 1979; Burek et al., 1980). In the latter study, rats were given either 0, 0.05, 0.2, 1.0, 5.0, or 20 mg acrylamide/kg/day via the drinking water. Rats given 20 mg/kg/day had marked neurotoxic effects and effects secondary to neurotoxicity with these effects noted clinically as early as the third week of the study. Histologically, these rats had moderate to severe degeneration of the peripheral nerves (specifically examined was the distal sciatic, i.e. tibial, nerve). Central nervous system (spinal cord) effects were also present but were equivocal to slight in degree. Effects in rats given 5.0 mg/kg/day were confined to the peripheral nerves and observed either histopathologically or by electron microscopy. Rats given 1.0 mg/kg/day had a minimal effect on the peripheral nerve observed only by electron microscopy.

The purpose of this study was to define the toxicologic and oncogenic effects of acrylamide when given to Fischer 344 rats in the drinking water for a period of two years. The study was designed and sponsored by American Cyanamid Company, Nalco Chemical Company, and The Standard Oil Company (Ohio) in addition to Dow Chemical U.S.A. The study included interim sacrifices after 6, 12, and 18 months and a subgroup of rats designated for electron microscopic examination of peripheral nerves to assess chronic neurotoxicity. This report details the observations from the rats designated for the two-year portion of the study.

METHODS

General Study Design. Groups of 90 rats/sex/dose group were given either 0 (controls), 0.01, 0.1, 0.5, or 2.0 mg acrylamide/kg body weight/day via the drinking water for up to 2 years. These doses were selected based upon the 13-week study previously cited. It was anticipated that the highest dose level (2.0 mg/kg/day) would produce a peripheral neuropathy detectable either by light or electron microscopy but not to the extent of being manifested clinically. Ten rats/sex/dose group were randomly selected for interim sacrifices after 6, 12 or 18 months on study. This selection occurred about 3 weeks prior to the respective interim sacrifice; any rats dying spontaneously prior to the selection process were thus automatically excluded from the interim sacrifice and conversely included as part of the group of 60 rats/sex/dose group designated for the 2-year terminal sacrifice[1]. The results of the interim sacrifices and related clinical determinations are reported separately (Gorzinski et al., 1984). Parameters monitored during the study included mortality, body weight, food consumption, water consumption, clinical observations, hematology, clinical chemistry, urinalysis, organ weights, gross and histopathology. The rats were started on test on 15 September 1980 and the terminal sacrifice was from 22-30 September 1982 (study days 738-746).

For another portion of the study, additional rats were given the above doses, sacrificed by intracardiac perfusion of glutaraldehyde-formaldehyde solution at various intervals, and subjected to an extensive examination of the nervous system including electron microscopy of the tibial nerve. Results from this electron microscopy portion will also be reported separately (Johnson et al., report in preparation).

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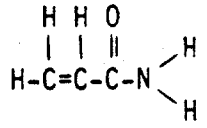
[1]One female rat given 2.0 mg/kg/day died the day prior to her scheduled necropsy at 18 months. This animal was not replaced for the interim sacrifice, thus leaving 9 female rats in the 2.0 mg/kg/day dose group at 18 months and 61 rats in this dose group for the terminal sacrifice.

Test Material. The sample of acrylamide (CAS No. 79-06-1) used for this study was purchased from Eastman Organic Chemicals Company, Rochester, N.Y. and was identified as No. X5521, Lot K7, enzyme grade. The chemical structure and selected properties are as follows:



Physical State:	Colorless, odorless crystals
	Tends to sublime, even at room temperature
Solubility:	Soluble in water, alcohol, acetone
	Insoluble in benzene
Specific Gravity:	1.122 (30°C)
Molecular Weight:	71.08
Vapor Pressure:	0.007 mm Hg (25°C)
Melting Point:	84.5°C

The bulk sample was stored in a freezer. An aliquot of the sample was recrystallized every 6 months for use in preparing the treated drinking water solutions for the corresponding time period. The aliquots were analyzed prior to use with the results reported in Table 1. Acrylamide content of the recrystallized samples varied from 96 to 99% with water being the major impurity (Table 1). Sequential analyses on the first aliquot confirmed its stability for up to 1 year. Accordingly, stability analyses on the other aliquots were not performed. During use, the aliquots were stored in containers placed in desiccators in a refrigerator.

Preparation and Analysis of Drinking Water Solutions. Previous data indicated that while acrylamide is stable in clean (tap) water for at least 7 days, when used in drinking water of rats there is a variable degree of degradation over this time period (Hermann and Momany, 1980). The extent of degradation was correlated with the degree of microbial growth, assumedly introduced from the rat's mouth when drinking. Modifications in the cleaning procedures used for water bottles also significantly reduced the extent of degradation. Therefore, the stability of acrylamide in drinking water was determined under the conditions actually used for this study (Morden et al., 1981a,b).

Acrylamide concentration was found to be at least 92% of the original concentration for at least four days under the system used for this study (16 oz. water bottle, 2 rats/cage). For this study, the drinking water solutions were prepared twice per week (every 3 or 4 days) by serially diluting a water concentrate (premix) prepared from a measured amount of the recrystallized test aliquot dissolved in a known volume of tap water. The targeted concentrations were based upon the mean body weight and water consumption of a subgroup of approximately 20 rats/sex/dose level as described under "Antemortem Observations and Measurements".

Analyses were frequently conducted on various drinking water preparations over the course of the study. The samples were analyzed by high performance liquid chromatography using a Radial-Pak C_{18} column, water eluent and UV detector at 200 nm (Campbell and Hermann, 1980). Analyses were obtained at the time a solution was prepared (day 0) from the dosing solutions used to fill the water bottles. For 190 samples taken over the course of the study from the dosing solutions (day 0) or the premix, the average was 99±7% of target concentration (data not shown).

Since some loss of acrylamide was anticipated from the drinking water after use, analytical effort was concentrated on drinking water samples selected at random after having been on the cage for 4 days (Table 2). An interfering peak (present from both control and treated rats in the water sample collected after 4 days on the cage) with the approximate retention time of acrylamide was noted for the first month of the study precluding accurate analyses during that period. Modifying the eluent to 10/90 methanol/water with 0.1M monobasic sodium phosphate eliminated the interference. This eluent was subsequently used on all samples taken after having been on the cage for 4 days. The frequency of analyses was adjusted to adequately establish the dose received by the test animals. Most of the analyses were conducted at the two lowest dose levels because other potential interferences would present the greatest potential to distort the results at these levels. Thus, clear definition of acrylamide level was considered most necessary at these levels. Additionally, Morden et al. (1981b) demonstrated slightly greater percentage of microbial degradation over a 7-day period at the lower dose levels in their test system.

For this study, the mean values ranged from 94% to 105% of targeted values for all dose levels over the course of the study. No acrylamide was detected in the 99 samples collected from control rats.

Test Animals and Husbandry. Male and female CDF Fischer 344 rats (Charles River Breeding Laboratory, Portage, Michigan) four weeks of age were purchased for the study.

Upon arrival at the laboratory[2], the rats were examined for health status and acclimated to the laboratory environment according to the Standard Operating Procedures of the Toxicology Laboratory.

Following acclimation (11 days), the rats were weighed and assigned to treatment groups using a computer-generated randomization program. Animals found to be outliers on the basis of their body weight (outliers identified by sequential method described by Grubbs, 1969) were discarded from the study. Animals from the extremes of the body weight distribution were identified and removed from the test population until only the number of rats required for the study remained. The animals remaining were ranked by body weight, divided into groups of five/sex, and one animal from each group assigned to each dose level. No animals were replaced during the study, all extra rats were removed from the study room after two weeks and were used as stock animals. Individual identification of all animals was accomplished by inserting a numbered metal ear tag in one ear of each rat.

The animals were housed (2/cage) in stainless steel cages having wire mesh floors in racks provided with deotized cageboard (DACB, Upjohn Company, Agricultural Division, Kalamazoo, Michigan) to minimize odor and aid in maintaining a clean environment. The cages contained a food crock and bails to facilitate positioning and securing the 16 oz glass water bottles used in the study. Animal cages were washed in accordance with good animal husbandry procedures. The water bottles were washed each time the solutions were

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[2]Fully accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC).

changed (every 3 or 4 days). The study was conducted in an environment designed for controlled humidity (40-60%), temperature (22±2°C), a 12-hour photocycle and an air change approximately every 5 minutes.

Food (Purina's Certified Rodent Chow #5002, Ralston Purina Co., St. Louis, Missouri) and drinking water solutions (water from the municipal water supply) were available ad libitum throughout the study.

Analysis on Purina's Certified Rodent Chow was performed by the Ralston Purina Company to confirm that the diet provided adequate nutrition, and to quantitate the levels of selected chemical contaminants. Analysis of tap water was performed according to the Standard Operating Procedures of the Toxicology Laboratory.

Antemortem Observations and Measurements. The rats were generally observed twice daily during the work week for overt signs of toxicity or changes in demeanor. These observations included the animal's movement within the cage, the availability of food and water, wastage of feed and the response to the opening and closing of the cage. Routine monitoring on weekends and holidays was limited to the removal of dead animals and animal husbandry procedures required to ensure the availability of food and water.

All rats were examined approximately monthly after the first month for palpable masses. During this examination, the length of the teeth was checked and the movement of selected animals observed when they were placed on a flat surface to assist in observing neuromuscular coordination.

Individual body weights were recorded monthly from all rats. A subgroup consisting of the first 20 rats (10 cages at study start) from each dose group was used to evaluate water and food consumption data. The subgroup was maintained near its targeted number of 20 rats with succeeding cages added as necessitated by mortality. The body weight and water consumption data from this subgroup were used to calculate the necessary acrylamide concentrations in the drinking water for their respective dose group. Data on these parameters were recorded weekly from the subgroup for the first 3 months on test; thereafter, body weights were recorded monthly and food and water consumption

one week of the month. Water consumption data were obtained at 3 and 4-day intervals with the 4-day data being used for the drinking water mixing instructions. After approximately 18 months on test, the mean group weight of all rats, rather than that of the subgroup, was used to calculate the mixing instructions.

Clinical Laboratory Studies. Hematologic evaluations[3] of packed cell volume (PCV), hemoglobin (Hgb), total erythrocytes (RBC), leukocyte count (WBC), platelet count (Plat) and red cell indices were performed on 10 randomly selected rats/sex/dose group. The blood samples were collected by orbital sinus puncture about 2 weeks prior to the terminal sacrifice. Stained blood smear examinations[4] and differential leukocyte counts were conducted on rats from the control and high dose groups.

Urine, collected on SARAN Wrap* by gently applying pressure on the inguinal area of the rat, was also collected when the blood samples were obtained. The urine was analyzed for specific gravity[5] and a semiquantitative estimate of pH, protein, glucose, blood, ketones, bilirubin, and urobilinogen[6].

Clinical chemistry parameters[7] evaluated from rats at the two-year terminal sacrifice were serum concentrations of urea nitrogen (BUN), total protein (TP), albumin (ALB), globulin (GLOB), glucose (GLUC) and activities of the following enzymes - alkaline phosphatase (AP), glutamic-pyruvic transaminase (SGPT), and chloinesterase (CHE). Blood for these determinations was collected

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[3]Hematology parameters measured with ELT-8, Ortho Instruments, Westwood, Massachusetts.

[4]Honeywell ACS-1000, Honeywell Institute, Denver, Colorado.

[5]TS Meter, American Optical Co., Keene, New Hampshire.

[6]Chemstrip 7, Urotron - Bio-Dynamics/BMC, Indianapolis, Indiana.

[7]Centrifichem System, Methods File, Union Carbide Corp., Rye, New York.

*Trademark of The Dow Chemical Company.

at necropsy from the severed cervical vessels from 10 rats/sex/dose level. The rats were the same 10/sex/dose level selected at random for the hematology and urinalysis examinations. If a selected rat died in the interval between collection of blood and urine specimens and necropsy, it was replaced by another rat selected at random.

Postmortem Observations and Measurements. All rats surviving until the terminal sacrifice were fasted overnight, weighed, anesthetized with methoxyflurane, the trachea exposed and clamped with a hemostat, and killed by decapitation[8]. A complete gross necropsy examination was performed by a veterinary pathologist. The eyes were examined using a moist microscope slide with fluorescent illumination. Following examination, the brain, heart, liver, kidneys and testes were excised, weighed, and the organ to body weight ratio was subsequently calculated for each. The tissues listed in Table 3 were collected and preserved in neutral, phosphate-buffered 10% formalin. Three pairs of peripheral nerves were dissected by fine dissection and placed in labeled cassettes to facilitate later identification. These nerves were the tibial branch of the sciatic nerve, the saphenous branch of the femoral nerve, and the brachial plexus. Specifically the tibial nerve was identified as that section of the ischiatic nerve extending from the knee (stifle) to the ankle (tarsal) joint. The entire spinal column was removed and transected to provide cervical, thoracic, and lumbosacral portions. Following examination, the lungs were distended to approximately normal inspiratory volume by tracheal instillation of formalin solution from a syringe with blunted needle canula. The nasal cavity was flushed with formalin solution delivered through the pharygneal duct.

Rats which died spontaneously or were sacrificed in a moribund condition were necropsied in a similar manner, except that final body and organ weights were not obtained. Due to the rapid onset of postmortem artifacts, a detailed eye examination was not performed on rats dying spontaneously.

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[8]Due to inadequate numbers of surviving rats in some dose levels from the electron microscopy portion of the study, a few rats were perfused in order to provide an adequate number of tibial nerve samples. This included: 2 males given 0, 1 female given 0.01, 1 male and 1 female given 0.1, 3 males and 2 females given 0.5, and 1 male given 2.0 mg/kg/day. Other than 1 tibial nerve, all other tissues were collected as described for the terminal sacrifice.

Representative sections of all tissues and organs listed in Table 3 (except the auditory sebaceous gland which was not routinely processed) were processed in a standard manner, embedded in paraffin, sectioned at 5-6μ, stained with hematoxylin and eosin, and examined histologically by a veterinary pathologist. As specified in the protocol, three different peripheral nerves (brachial plexus, saphenous branch of the femoral nerve, and the tibial branch of the sciatic nerve) were examined from 10 randomly selected rats/sex/dose group (the 10 being those from which blood samples were collected for clinical chemistry analyses). Tibial nerves, identified as the target organ, were examined on a "blind" basis from all rats over a short time interval. The nerves were subjectively graded into degrees of involvement based upon the number of focal degenerative lesions ("digestion chambers") present as follows: very slight - one to five digestion chambers; slight - six to fifteen digestion chambers, averaging less than one per high power (400X) field; moderate - numerous digestion chambers, often 2-3 or more per high power field; or severe - digestion chambers or overt loss of nerve fibers involving at least one-third of the fibers in the nerve. It should be emphasized that these grades refer to degree of histologic change and not clinical neuropathy. Five coronal sections of the brain were routinely processed. The spinal cord was examined at three different locations (cervical, thoracic, and lumbosacral) from all rats as specified in the protocol. Additional sections, either from the same embedded block or from additional pieces of fixed tissue, were occasionally prepared and examined to further clarify a gross or histopathologic observation. Based on histopathologic examination, additional sections of testes and epididymides (generally 4 of each organ) were examined from all male rats. Special stains were only infrequently used to assist in diagnosing some lesions. A complete inventory of tissues examined histologically is included with the histopathology tables.

Statistical Analysis. Consistent with laboratory policy, only descriptive statistics are reported for clinical laboratory data (after 18 months), and organ and body weight data from the terminal sacrifice. Results of statistical hypothesis testing are not presented for these parameters for the following reasons. These data are normally collected and analyzed for the detection and interpretation of non-neoplastic, chronic toxic effects of administration of

test substances. Compared to younger rats, older animals represent a characteristically diverse population, no longer accurately described by the above parameters. In the latter portions (after 18 months in the Fischer 344 rat) of a lifetime study there are numerous geriatric changes, notably neoplasms, present in a high proportion of the animals. Once an animal develops a tumor, a change in these parameters may be expected, but the nature and magnitude of such change is not predictable and the change is not necessarily representative of chronic changes in the group due to test material administration. However, the data are useful in evaluating the health status of individual rats, whether or not such status can be correlated with treatment.

Body weights, collected either weekly or monthly as noted above, were evaluated by analysis of variance (Steel and Torrie, 1960) for differences between groups. If the overal analysis of variance was significant (α=0.10) Dunnett's t-test (Winer, 1971) was used to identify statistically significant differences (α=0.05, two-sided) between experimental groups and their control.

Cumulative mortality data were tabulated monthly and analyzed for overall differences by the Gehan-Wilcoxon test (Breslow, 1970; α=0.05).

For histopathologic observations, treatment group comparisons of cumulative incidence were examined primarily by Fisher's Exact Probability Test (Siegel, 1956; α=0.05, one-sided). For observations with a control incidence of at least 6 percent, a Bonferonni correction (Miller, 1966) for multiple treatment-control comparisons was applied. For observations below a 6 percent background incidence, the true false-positive statistical error rate is well below the nominal 0.05 level set for Fisher's test, so no multiple comparison corrections were used.

In the absence of positive Fisher's test for a histopathologic lesion, the Cochran-Armitage test (Armitage, 1973; α=0.05, one-sided) for linear trend in incidence was performed, if the requirements for a valid chi-square statistic were met (i.e., no expected value less than 2.0).

Neither Fisher's nor the Cochran-Armitage test were applied to the tabulated category "within normal limits," nor on "secondary" tumors (metastatic sites). When multiple grades of a lesion were given, only the most advanced grade (or

a combination of the two most advanced grades when frequencies were low) and the total number of animals with the lesion were analyzed. This served to evaluate exacerbation of commonly-occurring lesions as a result of exposure.

Because there were significant differences in median survival times among treatment groups by the Gehan-Wilcoxon test, Fisher's test was supplemented by the mortality-adjusted comparison methods of Peto (1980), where these tests were deemed informative and valid (by the chi-square criterion above).

Water and food consumption are routinely not analyzed statistically. These data are normally collected primarily for calculation of mixing instructions and also for monitoring palatability problems and other concerns relative to administration of the test compound. Toxicologically, food and water consumption data may indicate a departure from the general "well-being" of an animal, but they must be critically evaluated to rule out the effects due to feeding habits alone.

Outlying values (α=0.02, two-sided) were identified by the sequential procedure described by Grubbs (1969). Outliers were identified but not excluded from the descriptive statistics calculated for the clinical laboratory data and the organ and body weight data from the terminal sacrifice. Outlying values were excluded from the values reported for body weight, food and water consumption. They were also excluded when mixing instructions were calculated.

The "palpable mass" and gross pathologic observations are intended primarily as an aid in histopathologic examination and diagnosis. Identical observations from either of these areas may occur with entirely different histopathologic lesions. These results are carefully evaluated but statistical analyses are considered inappropriate.

RESULTS

Antemortem Observations. The antemortem data is presented in the following summary tables and figures:

Parameter Evaluated	Table Number	Figure Number
Body Weights - Males	4	1
Body Weights - Females	5	2
Water Consumption - Males	6	
Water Consumption - Females	7	
Food Consumption - Males	8	
Food Consumption - Females	9	
Palpable Mass Observations - Males	10	
Palpable Mass Observations - Females	11	
Cumulative Mortality	12	3 & 4[9]

Male rats given the high dose of 2.0 mg/kg body weight/day had slight mean body weight suppression. This was first statistically identified on study day 89 and persisted for the remainder of the study. Over this time course, the extent of this difference gradually increased from about 2% less than controls on day 89 to a 3-4% difference after one year that was maintained for the remainder of the study. Males given 0.5 mg/kg/day had equivocal mean body weight suppression (usually 2% or less suppression) that was infrequently identified as statistically significant for the first 18 months on study. In the latter portions of the study their weight was similar or even heavier than controls. Male rats given the two lower dose levels were similar in body weight to controls throughout the study.

For female rats, there was no definitive change in body weight related to acrylamide ingestion. However, rats given the high dose of 2.0 mg/kg/day were generally the lightest group when weighed but this difference was minimal (the rats usually weighed 98% or more of the control group mean) and the mean

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[9]Figures 3 and 4 are actually cumulative survival as calculated by Kaplan-Meier method.

weight was rarely statistically significantly different from controls. Female rats ingesting the other three levels of acrylamide were similar or even slightly heavier than controls.

Food and water consumption values for male rats were similar to controls throughout the study. Female rats given 0.1, 0.5, or 2.0 mg/kg/day appeared to drink slightly more water than controls. This difference was slight (averaging approximately 1 gm water/rat/day) and was not related to the dose of acrylamide. The increase in water consumption was so minimal that it was not reflected by decreased urinary specific gravity at either the terminal (Table 18) or interim sacrifices (data not shown). The difference is of doubtful toxicologic significance. Female rats from these three dose groups also appeared to consume slightly more food daily (however, this averaged less than 0.5 gm/rat/day).

Clinical observations disclosed little apparent difference between dose groups. On study day 210 some rats from all dose groups were noted to have excessive lacrimation and enlarged salivary glands consistent with sialodacryoadenitis virus (SDA) infection and the study room was quarantined by the clinical veterinarian. All groups, males and females, appeared to be equally affected. The swollen salivary glands resolved within a period of three days. Photophobia and excessive lacrimation persisted for about 10 days, with a declining incidence. Mean body weights from day 213 were decreased 11-12 gm from the previous month for all groups of male rats; while mean body weights for female rats were essentially the same as the previous weighing. The only mortality during this interval was a male rat given 0.5 mg/kg/day. The cause of death was not related to SDA virus infection and the salivary and lacrimal glands were within normal limits histopathologically. The quarantine was removed after 30 days.

Observations of palpable masses were infrequent until the last few months of the study. The majority of masses observed clinically were subsequently diagnosed histopathologically as tumors originating from the skin or the subcutaneous tissues and glands (especially mammary gland). Inspection of Table 10 discloses no readily apparent differences between controls and rats

given 0.01, 0.1, or 0.5 mg/kg/day. Rats given 2.0 mg/kg/day appeared to have a slightly increased number of palpable masses over the last 4 months of the study (Table 11).

There were no apparent treatment effects on mortality until the 21st month of the study. Up to that time, spontaneous deaths appeared to be random and the groups having the highest mortality were the males given 0.01 mg/kg/day and the females given 0.1 mg/kg/day. From 21 months until termination there was increased mortality in rats given 2.0 mg/kg/day such that by the end of the study there was significantly increased mortality for both sexes. Increased mortality was not present in any of the other treatment groups. Although female rats given 0.5 mg/kg/day had several more deaths than controls (17 vs. 10) it should be noted that mortality in this dose group is near the historical control average of 25% for control female F344 rats after 24 months on study in our laboratory (Frauson and Bell, personal communication) as well as that indicated by other investigators (Solleveld et al., 1984).

Clinical Laboratory Studies. Summary tables from the clinical laboratory studies are presented as follows:

Parameter Evalated	Table Number
Hematology - Males	13
Hematology - Females	14
Clinical Chemistry - Males	15
Clinical Chemistry - Females	16
Urinalysis - Males	17
Urinalysis - Females	18

As noted in the methods section, evaluation of mean clinical laboratory data gathered at the terminal sacrifice for chronic toxicologic effects due to treatment is difficult due to disparities within the aged population. Spontaneous disease processes, even though they may occur in a low number of rats, may dramatically affect group means. Additionally, the extent of change in laboratory values may be markedly different in rats having the same disease process. Therefore, clinical laboratory values must be correlated with gross

and histologic diagnoses on an individual animal basis, as well as the overall incidence pattern, before one accepts any apparent difference as being due to test compound administration.

In this study there were no changes in the clinical laboratory data which were attributed as primary effects of acrylamide ingestion. While there may be some apparent differences in a few of the values, correlation with the gross and histologic observations on an individual basis (data not presented) provides an explanation for the changes. The differences noted in the clinical laboratory summary tables (e.g., the erythron of female rats given 2.0 mg/kg/day, SGPT and AP values in this same group) are largely due to other conditions which affect these values. Specifically, Fischer rat leukemia may profoundly affect the erythron in addition to the white blood cells (Stromberg et al., 1983b). Liver involvement, frequent in this leukemic syndrome, may cause elevations of serum enzymes (Stromberg et al., 1983c). Thus, even though the incidence of Fischer rat leukemia was similar in females given 2.0 mg/kg/day to controls (see Table 24, p. 213) a disproportionate number of these leukemic rats were present in the selected females given 2.0 mg/kg/day. Secondly, there was marked variation in the degree of change of the clinical laboratory values among the leukemic rats which also influenced the group means. Lastly, effects attributed to acrylamide treatment were not present in clinical laboratory tests when sampled at 3, 6, 12, or 18 months (Gorzinski et al., 1984).

Postmortem Observations and Measurements. Summary tables of observations and measurements made at necropsy and upon tissue specimens collected at that time are presented as follows:

Parameter Evaluated	Table Number
Organ/Terminal Body Weights - Males	19
Organ/Terminal Body Weights - Females	20
Gross Pathologic Observations - Males	21
Gross Pathologic Observations - Females	22
Histopathologic Observations - Males	23
Histopathologic Observations - Females	24
Summary of Tumor Incidence	25
Observations Suggestive of Tumors For Which No Final Diagnosis Was Made	26

The gross and histopathology tables are divided such that, in addition to the cumulative total rats having a specified observation, the number occurring in rats from the terminal sacrifice as well as early deaths (either spontaneous deaths or sacrificed in moribund condition) at various time intervals may also be examined. Additionally, when specific diagnoses are discussed, the table and page number will be referenced for the convenience of the reader due to the voluminous nature of these tables.

The fasted body weight of rats at the terminal sacrifice were consistent with the previously reported monthly body weights. Male rats given 2.0 mg/kg/day weighed about 4.6% less and female rats at this dose level weighed about 2.1% less than their respective controls. Treated rats from all other dose levels had mean fasted body weights greater than controls.

The liver weights, both absolute and relative, were increased in male or female rats given 2.0 mg/kg/day. The reason for this increase was not apparent and its toxicological significance is doubtful. Similar increases were not present at any of the interim sacrifices except for male rats at the 6-month interim sacrifice. There were no gross or histopathological correlates to this observation at the terminal sacrifice. Absolute and relative weights of the other organs reflected expected variability with no differences ascribed to acrylamide ingestion.

Gross observations are primarily made to assist in the selection of samples for histopathology and interpretation of those sections and cannot stand by themselves. Therefore, the gross diagnoses, as reported in Tables 21 and 22, are considered preliminary and one must be thoroughly familiar with the diagnostic terms employed at any specific laboratory as well as have a basic knowledge of the background incidence of certain lesions in the test strain and species before making definitive assessments. Remembering this basic tenet, the only gross observation for which one would assume a correlative histopathological diagnosis that showed a possible response to acrylamide treatment was for masses collectively identified in either the mammary gland (Table 22, p. 137) or skin (Table 22, p. 116) of female rats. Examination of individual animal necropsy records disclosed that several of the masses tabulated with "external and skin"

to be likely of mammary origin based on location (subcutis, trunk, or ventral areas of animal) and description (usually pale, firm, circumscribed, multilobular). These occurred as follows:

Female Rats	Dose (mg/kg/day)	1-18 Months	19-24 Months	Terminal Sacrifice
External and Skin Mass/Nodule	0	1(0)[a]	2(0)	0
	0.01	1(0)	0	0
	0.1	1(1)	1(0)	1(0)
	0.5	0	2(0)	0
	2.0	2(2)	5(4)	0

[a]Number is the number of rats having the stated observation. Number in parentheses is the number considered likely to be of mammary origin based on description and comments at necropsy.

Thus, the total rats considered on the basis of gross examination to have a mass of likely mammary origin are as follows:

Female Rats	Dose (mg/kg/day)	1-18 Months	19-24 Months	Terminal Sacrifice	Cumulative Results
Total rats with one or more mammary masses or external and skin mass likely of mammary origin	0	0	1	7	8
	0.01	0	1	10	11
	0.1	1	0	8	9
	0.5	0	6	12	18
	2.0	2	13	10	25

Therefore, it appeared that there was an increase in mammary masses as diagnosed at necropsy in female rats given 2.0 mg/kg/day. There appeared to be an equivocal increase in female rats given 0.5 mg/kg/day.

At the terminal sacrifice, specific attention was directed to the plantar surface of the rear feet. It was reasoned that a slight degree of neuropathy, such that it might not be recognized on routine clinical examination, might be apparent in lesions of the rear feet or foot pads. Older rats frequently have lesions of the feet including calluses (verrucous thickening), scabs, or abscesses,

possibly due to the wire mesh cage floor. When these diagnoses are reviewed for this study (Table 21, p. 79; Table 22, p. 115), it is clear that there was no difference that could be ascribed to acrylamide treatment.

Histopathology. Only those histopathologic findings considered treatment related or biologically relevant will be discussed.

Non-Neoplastic Diagnoses. Degeneration of peripheral nerves was noted to be increased, as expected, in rats given 2.0 mg/kg/day (Table 23, pp. 142-143; Table 24, pp. 200-201). This treatment effect was best demonstrated for the tibial nerve, a distal peripheral nerve, which was examined from all rats on study. The saphenous nerve, also a distal portion of nerve, and the brachial plexus, which is a more proximal portion from the front limb, were examined from only 10 rats surviving to the terminal sacrifice. The saphenous nerve had apparent treatment-induced degeneration in males given 2.0 mg/kg/day but not females. No treatment effects were noted in the brachial nerves of females but there was a trend suggesting an effect in males receiving 0.1 mg/kg/day or more. This possible effect at lower dose levels than was noted for the tibial nerve was considered of questionable validity because of the small number of rats examined.

The effect on peripheral nerves consisted of focal degeneration of individual axons and their myelin sheaths. Usually this was noted as a vacuolated phagocyte containing debris ("digestion chamber"). Each nerve was examined on a blind basis and was graded on a scale of very slight to severe based on the frequency of these changes as noted in the Methods section. It should be remembered that these grades do not correlate with clinical changes. Some degree of nerve degeneration was noted in most rats (including controls) on study with the males having slightly greater incidence and severity than females. This is considered a spontaneous geriatric change and has been reported by others (Van Steenis and Kroes, 1971, Cotard-Bartley et al., 1981). The peripheral nerve degeneration noted in acrylamide treated rats represents an increase in frequency or severity over the control group as opposed to an all-or-none effect. Similar effects had been noted at both the 12- and 18-month interim sacrifices on this study, especially for male rats given 2.0 mg/kg/day.

Aged rats also have spontaneous degenerative changes of the spinal cords and nerve roots (Van Steenis and Kroes, 1971; Burek et al., 1976; Krinke et al.; 1981, Mitsumori et al., 1981). Although acrylamide has been noted to produce degenerative changes in spinal cord axons at higher dose levels, there was no increase in the frequency or degree of degenerative changes noted in the spinal cord at the dose levels used in this study (Table 23, pp. 146-149; Table 24, pp. 204-207). Actually, there was a slight decrease in degenerative changes in the lumbosacral portion of the spinal cord of rats given 2.0 mg/kg/day.

The livers of treated rats tended to have multiple areas of altered hepatocytes (Table 23, p. 150; Table 24, p. 208), whereas controls has an increased number of rats having only a single area. The total number of rats having one or more areas of altered cells was essentially similar between treated and control rats. This observation was regarded as being of minor toxicologic significance.

Foci of altered cells were frequently present in the cortex of the adrenal glands. The foci generally consisted of spherical groups of vacuolated cells but groups of eosinophilic or basophilic cells were also noted. While the overall incidence of rats having these foci was similar between controls and treated, multiple foci were more common in treated rats, while single foci were more common in controls (Table 23, p. 162; Table 24, p. 218). The toxicologic significance of this observation is unknown but is considered minimal. Some authors have considered these foci to be focal hyperplasia (Strandberg, 1983). Only one adrenal cortical tumor was present in this study (a female rat given 2.0 mg/kg/day) despite the number of rats having these foci.

There are several other observations of a non-neoplastic nature noted on Tables 23 and 24 to be statistically different from the control group. These were regarded as being of little toxicologic significance for one or more of the following reasons:

1. The lack of an apparent dose-response relationship.
2. They represent a decreased incidence of a lesion.
3. They are considered secondary effects of lesions not related to treatment or secondary to treatment-related tumors to be discussed.
4. They are minor changes perceived to be within expected incidence ranges for untreated rats of this strain and age.

Neoplastic Observations. Several types of tumors occurred with increased incidence in acrylamide treated rats. In females this included tumors of the mammary gland, central nervous system, thyroid gland, oral tissues, clitoral gland and uterus. In males, increased incidences of tumors were found in the thyroid gland and the scrotal mesothelium.

Most of the mammary masses noted grossly (as well as those grossly coded as skin which were considered of likely mammary origin) were diagnosed histopathologically as some form of mammary tumor. The most frequent tumor was composed of a proliferation of mixed connective tissue and glandular elements typical of a fibroadenoma, a benign tumor. However, the relative proportion of these elements varied such that some tumors consisted almost solely of glandular elements and were diagnosed as adenomas. Others, frequently the largest tumors, were diagnosed as fibromas based on connective tissue being the sole component. Based on this variability in histopathologic appearance, these diagnoses were tabulated separately by specific type as well as total benign mammary tumors. Female rats given 2.0 mg/kg/day had increased numbers of fibromas alone and also total benign mammary tumors (Table 24, p. 243-244). Female rats given 0.5 mg/kg/day had increased numbers of benign tumors (Total 10/60 controls, 19/58 rats given 0.5 mg/kg/day) but this increase was not statistically significant. The control rate of 17% (10/60) is near the historical control average of 18% for this laboratory but is lower than the figure given by the National Toxicology Program of 24.1% (572/2370) (Solleveld et al., 1984).

The majority of the benign mammary tumors were diagnosed from female rats at the terminal sacrifice. However, two benign tumors occurred in rats given 2.0 mg/kg/day prior to 18 months on study (a fibroadenoma in a rat sacrificed in moribund condition on day 492 and a fibroma in a spontaneous death on day 481). Additionally, there were increased numbers of benign tumors for female rats given 2.0 and possibly 0.5 mg/kg/day in the interval from 22 months to the terminal sacrifice.

Mammary adenocarcinomas, malignant tumors derived from the glandular epithelium, were increased in female rats given 2.0 mg/kg/day. Statistically this was noted to be a positive linear trend but the only dose group for which there were increased tumors was the group given 2.0 mg/kg/day. Malignant mammary tumors occurred 2.1% of 2,370 control female Fischer rats in the NTP.

Malignant mammary tumors were diagnosed only at the terminal sacrifice for control female rats or those given 0.01, 0.1 or 0.5 mg/kg/day. However, for females given 2.0 mg/kg/day, only 1 of 6 occurred at the terminal sacrifice. The other 5 occurred in rats dying spontaneously in the final 6 months of the study, with the first from a rat dying on day 577.

For male rats, mammary tumors (Table 23, p. 188) were histologically similar to those in females. Fibromas of mammary origin were diagnosed more frequently than fibroadenomas. Malignant tumors (adenocarcinomas) were not present in males. There were no statistical differences in mammary tumor incidences in male rats.

Tumors of glial cell origin were noted in both the brain and spinal cord of males and females (Table 23, p. 145-148; Table 24, p. 202-206). The most frequent of these tumors were diagnosed as astrocytomas. These were relatively large, cellular masses that replaced sizable portions of nervous tissue and were frequently present on more than one of the five coronal sections of brain even though they were rarely noted grossly. These tumors consisted of dense collections of cells having round to oval nuclei with uniform pale nucleoplasm. The oval nuclei often had a folded nuclear membrane. In the spinal cord, these tumors often had oval or fusiform nuclei, many of which were folded. The cytoplasm was eosinophilic and was usually ill-defined but at times the cells appeared fusiform. Mitoses were generally uncommon. At the tumor margins, tumor cells were preferentially localized around neurons (satellitosis) or blood vessels.

Oligodendrogliomas, a second type of glial tumor, consisted of masses of cells with round nuclei. These varied from small dense nuclei to larger vesicular ones. Cytoplasm was usually ill-defined around the small nucleated cells, whereas the larger nuclei frequently had a thin rim of pale cytoplasm. These tumors were characterized by clear spaces around the cells producing a "honeycomb" appearance. Necrosis was more commonly associated with oligodendrogliomas than with astrocytomas.

Another proliferative lesion of glial cells noted in some rats consisted of microscopic foci characterized by perineuronal and perivascular accumulations of cells (probably astrocytes). These cells generally had irregular oval nuclei

and indistinct cytoplasm. As opposed to the astrocytomas, the basic tissue architecture remained discernible in spite of the increased cell density. On serial recuts, these foci diminished. This lesion was considered an atypical proliferation (i.e., not a response to injury). While these foci may represent an early astrocytoma, they were coded as glial proliferation (suggestive of early tumor) in recognition of the fact that other pathologists may have a different opinion as to their neoplastic status. However, their potential as small tumors should be recognized when evaluating the results. One consulting veterinary neuropathologist has stated that he considers these lesions to be astrocytomas (Friedman, 1983).

These glial tumors or proliferations were presented under several different tissues (brain or various locations of the spinal cord) in Tables 23 and 24. The cumulative incidence for these tumors in the central nervous system of female rats is:

	Dose (mg/kg/day)				
	0	0.01	0.1	0.5	2.0
Brain					
Astrocytoma	0	1	0	0	3
Glial proliferation (suggestive of tumor)	0	0	0	1	3
Oligodendroglioma	0	1	1	0	1
Spinal Cord (Cervical, Thoracic, and Lumbosacral)					
Astrocytoma	1	0	0	0	3
Total rats with a tumor of glial origin or a glial proliferation suggestive of early tumor	1	2	1	1	9[a]

[a]One female rat given 2.0 mg/kg/day had an astrocytoma in the cervical section of the spinal cord and glial proliferation in the brain.

Considered individually, each of the various categories have no statistical significance. However, when they are combined, female rats given 2.0 mg/kg/day have an increased incidence of total glial tumors. Additionally, other combinations were also statistically significant (i.e., astrocytomas from brain and

cord or astrocytomas and glial proliferation from brain and cord). It is deemed biologically appropriate to combine equivalent diagnoses from the brain and spinal cord as the distinction made in the tables artifactually separates what is considered a similar response to treatment.

Glial tumors or proliferations in control rats were found only from those surviving until the terminal sacrifices. For female rats given 2.0 mg/kg/day, the earliest tumors were an astrocytoma for the lumbosacral cord from a moribund rat on day 492 and a brain astrocytoma from a moribund rat on day 610. For females given 0.01, 0.1, or 0.5 mg/kg/day, the only tumor diagnosed prior to the terminal sacrifice was an oligodendroglioma from a rat given 0.01 mg/kg/day and sacrificed in moribund condition on day 733.

The cumulative incidence for glial tumors of the central nervous system of male rats is:

	Dose (mg/kg/day)				
	0	0.01	0.1	0.5	2.0
Brain					
Astrocytoma	3	0	0	2	2
Glial proliferation (suggestive of early tumor)	0	0	0	1	1
Oligodendroglioma	0	2	0	0	1
Spinal Cord (Cervical, Thoracic, and Lumbosacral					
Astrocytoma	1	0	0	0	3
Undifferentiated glial cell tumor	1	0	0	0	0
Glial proliferation	0	0	0	0	1
Total rats with a tumor of glial origin or a glial proliferation suggestive of early tumor	5	2	0	3	8

Glial proliferations and tumors of the CNS of male rats showed no significant dose-response relationship. However, the incidence of astrocytomas in control males greatly exceeds historical controls. In our laboratory, the historical average is 1.0% (3/306) (range 0 - 2.3%) for control male rats and 0.6% (5/827) (range 0 - 2.3%) for all male rats of this strain from 24 or 27 month studies. The NTP reports a historical control incidence of <1% for 2320 rats (Solleveld et al., 1984). One reason for the increased number of tumors observed in this control group may be the expanded number of sections examined from the rats in

this study. While this may have been a factor for the spinal cord tumors, this was considered unlikely for the brain tumors as they were usually large enough to be present in the three sections routinely taken at this laboratory. The number of small glial proliferations (suggestive of early tumor) may be influenced by the number of sections examined; however, these were not present in controls. It is the opinion of the authors that the increased number of brain tumors present in male rats given 2.0 mg/kg/day is likely a response to treatment even though it lacks statistical significance when compared to the concurrent control group.

All glial tumors from control male rats were observed in animals from the terminal sacrifice. The earliest tumors from treated rats were a brain astrocytoma from a rat given 0.5 mg/kg/day and sacrificed on day 212 and a brain oligodendroglioma from a rat given 0.01 mg/kg/day and dying on day 411. The earliest glial tumors in male rats given 2.0 mg/kg/day were an astrocytoma in the thoracic spinal cord of a rat dying on day 561 and a brain astrocytoma from a rat dying on day 680.

The only tumor type for which there was a statistically significant increased incidence for both sexes was for tumors derived from the follicular epithelium of the thyroid gland (Table 23, p. 183; Table 24, p. 240). In females, some of these tumors were diagnosed as being of low-grade malignancy; however, one should note that thyroid follicular tumors pose difficulty in classifying benign and malignant tumors (Napalkov, 1976). Though some tumors were called malignant, definite infiltration of adjacent tissue or distal metastases were not noted. In males, all tumors were considered benign. The tumors occurred in the latter stages of the study or at the terminal sacrifice. In females, the only tumors diagnosed prior to the terminal sacrifice were a papillary adenoma from a moribund rat given 2.0 mg/kg/day and sacrificed on day 705 and an adenocarcinoma from a moribund rat at this dose level on day 737. The earliest tumor in males was from a rat given 2.0 mg/kg/day and sacrificed in a moribund condition on day 663. Additionally, there was a slight increase (not statistically significant) in the incidence of rats given 2.0 mg/kg/day with cystic dilatation of the follicles, a lesion that has been considered as follicular cell hyperplasia by some investigators (Boorman, 1983). Most thyroid tumors in the Fischer 344 rat originate from the parafollicular cells (C-cells). Acrylamide treatment had no effect on the incidence of parafollicular cell tumors.

Tumors originating from the mucosa of the mouth are located under the tissues "tongue" or "oral tissues" on Tables 23 and 24 (p. 191-192 and p. 248-249), respectively. However, this is an artificial distinction due to histology preparation and tabulation (they are on different slides) and these should be added together to assess incidence of tumors in this region. When this is done, the incidence is:

	Dose (mg/kg/day)				
	0	0.01	0.1	0.5	2.0
Female rats					
Squamous papillomas, benign, origin from tongue, hard palate, or lip	0	3	2	1	7
Squamous cell carcinoma, malignant, origin from hard palate or gingiva	0	0	0	2	1
Male rats					
Squamous papillomas, benign, origin from tongue, hard palate or lip	4	7	0	5	4
Squamous cell carcinoma, malignant, origin from tongue, hard palate, gingiva or pharynx	2	0	1	0	2

All tumors occurred in separate rats (i.e., no rat had 2 papillomas, each in a different location, or a papilloma and a squamcus cell carcinoma).

The only finding of statistical significance is the papilloma in females given 2.0 mg/kg/day. The apparent disparity in response between males and females is unexplained. The incidence of these tumors in female rats appears low with the historical control average in this laboratory being 2.2% (range 0 - 4%) for squamous papillomas and 0.5% (range 0 - 1.2%) for squamous cell carcinomas of the oral cavity. In the same studies, the incidence was 0.5% (range 0 - 1.2%) for either squamous papillomas or carcinomas originating in the tongue. Focal epithelial hyperplasia (Table 23, p. 192-193; Table 24, p. 248-250) originating from the oral mucosa was also slightly increased in rats given 2.0 mg/kg/day (statistically significant only for males).

Female rats given 2.0 mg/kg/day had increased incidence of uterine adenocarcinomas, a malignant tumor originating from the glandular elements (Table 24, p. 230). These tumors were all diagnosed in rats from the terminal sacrifice

except for one rat given 2.0 mg/kg/day which was sacrificed in moribund condition on day 677. Uterine adenocarcinomas are uncommon lesions in Fischer 344 rats; the historical control incidence being 2.3% (range 2.0 - 2.3%) in this laboratory. The more common uterine tumor, endometrial stromal polyp (Table 24, p. 230-231) was present at all dose levels with the two higher treatment groups actually having a slightly lower incidence than the controls.

Benign tumors (adenomas) arising from the clitoral gland were increased for female rats given 2.0 mg/kg/day (Table 24, p. 246). Additionally, two malignant tumors and two benign tumors from this gland were diagnosed in rats given 0.5 mg/kg/day. This suggests a possible effect at this dose level although it lacks statistical significance. However, it should be noted that the lack of these tumors in the control rats is unusual. The historical control incidence in our laboratory is 0.5% for adenomas and 1.1% for adenocarcinomas. The NTP reports historical incidence rates of 1.2% for adenomas and 1.9% for carcinomas (Solleveld et al., 1984). In males, the preputial gland (analogous to the clitoral gland) showed no tumorigenic effect, there being adenomas in only one control male and one male given 0.01 mg/kg/day and a carcinoma in one male given 2.0 mg/kg/day (Table 23, p. 189).

There was an increased incidence of tumors originating from the mesothelium of the scrotum (tabulated under the testes, Table 23, p. 173). These tumors were usually multicentric. These tumors were regarded as non-metastatic when they were confined to the scrotal cavity (involving testes, epididymis, and the parietal mesothelium) while metastatic tumors had diffuse involvement of the abdominal cavity. Rats with abdominal involvement frequently were presented to necropsy with a distended abdomen due to serosanguineous or dark, bloody fluid. As noted in the Methods section, after completion and tabulation of the original sections, additional sections of the testes and epididymides were procured from the fixed tissues to better understand the incidence of these lesions. The results reported in Table 23 include these recuts. Most small tumors originally diagnosed were confirmed on the reexamination (i.e., additional sites of involvement were found), additional mesotheliomas were found for 2 rats given 0.5 and 1 rat given 2.0 mg/kg/day. These were small lesions but usually were noted in more than one of the multiple sections of tissue.

The mesotheliomas appeared typical of those previously described for Fischer 344 rats (Gould, 1977; Berman and Rice, 1979). Their earliest manifestation was usually as delicate fibrovascular papillary fronds covered with a layer of basophilic cuboidal mesothelial cells. Mitotic figures were infrequent. Larger or disseminated tumors were composed of larger fronds, plaque-like masses, and solid aggregates of mesothelial cells. The smaller masses did not have appreciable accumulations of inflammatory cells or fibroplasia as might be expected if these were a response to irritation. The larger disseminated tumors often had hemosiderin-laden macrophages and other inflammatory cells.

The incidence of mesothelioma was significantly increased in males given 0.5 or 2.0 mg/kg/day. However, this was not a typical dose reponse in that there was actually one less rat with mesothelioma in the group given 2.0 mg/kg/day than those given 0.5 mg/kg/day. Rats given 0.1 mg/kg/day appeared to have an increased incidence of mesothelioma (11.7% vs. 5% in controls), although this incidence was not statistically increased. Our historical incidence is 3.8% (range 2 - 6%) for control males at 24 months, while it is 4.9% (range 2 - 12%) for all male rats. The NTP breaks down mesotheliomas into two categories. They cite an incidence of 1.3% for mesothelioma of the testes and 1.0% for mesothelioma of the peritoneal cavity (Solleveld et al., 1984).

Most of the mesotheliomas were diagnosed from rats at the terminal sacrifice. Those occurring prior to the terminal sacrifice occurred late in the study and the proportion occurring early was similar among all dose groups. The earliest mesothelioma was diagnosed for a male rat given 0.5 mg/kg/day and dying on day 646. The earliest mesothelioma in a control male was for a rat sacrificed on day 681; that for a male given 0.1 mg/kg/day was for a rat sacrificed on day 674, and that for males given 2.0 mg/kg/day was on day 680.

On the additional sections, another mesothelial lesion was observed. This was tabulated as "reactive mesothelium with or without chronic inflammation" (Table 23, p. 173). This was usually observed histologically at the attachment of the epididymis to the testes (epididymal ligament). Although the surface mesothelium was basophilic and cuboidal, these were not associated with papillary fronds as noted in the small tumors. These were usually dome-shaped

foci associated with an inflammatory response. These were considered likely a response to irritation, possibly tension on the epididymal ligament due to an enlarged testis having a Leydig cell tumor. The incidence of this lesion did not show any relationship to acrylamide treatment.

Two types of benign tumors, pituitary adenomas in females and adrenal pheochromocytomas in males, were statistically identified as being increased but this is considered as being of questionable biological validity.

Tumors of the pituitary gland are the most common tumor of aged Fischer 344 female rats. The historical incidence of benign tumors (adenomas) in control female Fischer 344 rats from 24-month studies in this laboratory is 35.7% (range 28.2 - 46%), while the incidence for malignant tumors (adenocarcinomas) is 12.4% (range 8 - 20%). The NTP cites an incidence of 44% (range 18 - 70%) for adenomas and 3.5% (range 0 - 19%) for adenocarcinomas (NTP, 1983). In this study, adenomas were identified as being increased in female rats given 2.0 mg/kg/day (Table 24, p. 214). However, it should be noted that there was essentially no dose response (identical numbers of adenomas were present in rats given 0.1 mg/kg/day) and malignant pituitary tumors (adenocarcinomas) were actually slightly less in rats given 2.0 mg/kg/day than controls (5 vs. 7). Additionally, the incidence in the treated rats is similar to some of the historical control groups cited previously. While the significance of the number of pituitary tumors is questioned, it should be noted that those present were generally noted earlier (from incidence pattern on Table 24) and were larger than those in the control group. At gross necropsy, the diagnoses that usually correspond to pituitary tumors are dark foci for the smaller tumors and mass/nodule for the larger tumors. Grossly more female rats given 2.0 mg/kg/day (as well as all other treatment levels) were noted to have pituitary mass/nodules, whereas controls usually had dark foci (Table 22, p. 122).

In male rats, which have fewer pituitary tumors, there were less pituitary adenomas (Table 23, p. 157) in the rats given 2.0 mg/kg/day than in controls (17 vs. 22).

Benign pheochromocytomas, tumors arising from the adrenal medulla, were noted to be statistically increased in male rats given 2.0 mg/kg/day (Table 23, p. 161). However, in this instance, the control incidence appears low. The historical incidence in this laboratory is 7% (range 1.2 - 12%), while that of the NTP is 17.9% (Solleveld et al., 1984). Additionally, malignant pheochromocytomas were decreased in male rats given 2.0 mg/kg/day (0 vs. 2 in control males), and the combined incidence of benign and malignant pheochromocytomas was not statistically significant. For female rats there were too few pheochromocytomas to make any valid assessments on the effect of treatment; however, there were none in the females given 2.0 mg/kg/day vs. one in the controls.

DISCUSSION AND CONCLUSIONS

Throughout the major in-life portion of this study, acrylamide treatment was associated with only slight toxicologic effects attributed to treatment. Mean body weights were slightly decreased in male rats given 2.0 mg/kg/day (reaching about a 4% depression after 1 year on study and maintaining that level thereafter). Body weights were equivocally decreased (≈2%) in females at that dose level and males given 0.5 mg/kg/day.

Food and water consumption over the course of the study and clinical laboratory studies, organ weights, and organ/body weight ratios from rats at the terminal sacrifice added little information of toxicologic significance.

In the final months on the study, rats given the top dose level of 2.0 mg/kg/day had an increased incidence of palpable masses (generally subcutaneous) and increased numbers of rats dying spontaneously or sacrificed in moribund condition. By the termination of the study, mortality was significantly increased for both males and females receiving 2.0 mg/kg/day.

The expected slight peripheral neuropathy was present in rats given 2.0 mg/kg/day. This effect was detectable only by microscopic examination and clinical neuropathy was not present. Peripheral neuropathy was more apparent in male rats; however, they also had greater incidences of spontaneous degenerative lesions of the peripheral nerves. Minimal neuropathologic effects in males given 2.0 mg/kg/day were identified only by electron microscopy after 3 and 6 months on test. After 12 months, the effects were noted both by light and electron microscopy for both sexes. After 18 and 24 months of treatment, the small sample size and background incidence of degenerative neuropathy made interpretation of electron microscopy data (males only examined) complicated, although effects were still demonstrated by light microscopy.

Histopathologic examination disclosed increased incidences of tumors of several organs in treated rats. In female rats, there were increased incidences of tumors in the mammary gland (benign and malignant), central nervous system (malignant), thyroid gland-follicular epithelium (benign and malignant

combined), mouth (benign); clitoral gland (benign) and uterus (malignant). Male rats had increased incidences of tumors originating from the scrotal mesothelium (malignant) and the thyroid gland-follicular epithelium (benign).

Central nervous system tumors in males were not statistically increased; however, the control group greatly exceeded historical control averages and ranges. In view of this, the increase in central nervous system tumors in treated male rats given 2.0 mg/kg/day was considered biologically to be a treatment effect.

Conversely, tumors of the pituitary gland (benign) in female rats and the adrenal gland-medulla (benign) in male rats that were statistically identified as being increased in the 2.0 mg/kg/day dose group were considered of questionable biological validity based on historical data and actually decreased numbers of malignant tumors of these organs in the treated rats.

The total number of rats with tumors, or benign or malignant tumors, is presented in Table 25. Both males and females given 2.0 mg/kg/day have an increased incidence of total tumors, benign tumors, and malignant tumors. At dose levels of 0.5 mg/kg/day or less, tumorigenic effects are not apparent when one considers the total tumor incidence. For the specific tumor types noted above, all were increased in rats given 2.0 mg/kg/day. The only tumor statistically significantly increased in rats given 0.5 mg/kg/day was the scrotal mesothelioma in male rats. Though not statistically significant, benign mammary tumors and combined benign and malignant clitoral gland tumors were of increased incidence in females given 0.5 mg/kg/day.

At 0.1 or 0.01 mg/kg/day, there were no tumors that were statistically significantly increased. However, the scrotal mesothelioma in males given 0.1 mg/kg/day is increased above the concurrent or historical control values. Although not statistically significant, the increase at the higher dose levels suggests that the increased incidence at 0.1 mg/kg/day may represent a response to acrylamide treatment. However, there cannot be an unequivocal resolution to this question in view of the statistical power of the experiment and the incidence experienced by the concurrent controls. It should be noted that this tumor, in rats, has generally been considered as a malignant tumor with

benign forms not generally being recognized. Although they are rare, benign mesotheliomas have been reported in man (Whitaker et al., 1982). It should be noted that most of the mesotheliomas in this study were restricted to the scrotal cavity and some were very small proliferations. The major difference between the disseminated (metastatic) forms and the scrotal mesotheliomas appeared to be primarily tumor bulk rather than histologic indicators of anaplasia among the mesothelial cells. Thus, the inclusion of all mesotheliomas as malignant appears consistent with current concepts on the potential biological behavior of these tumors in Fischer 344 rats (Gould, 1977 and Berman and Rice, 1979).

The scrotal mesothelium of Fischer 344 rats appears unique in its ability to give rise to tumors either spontaneously or when treated with chemical carcinogens. Even when methyl (acetoxymethyl) nitrosamine was injected into the abdominal cavity, the induced mesotheliomas arose from the more remote peritesticular (scrotal) mesothelium rather than from the abdominal mesothelium (Berman and Rice, 1979). In the present study, the only mesothelioma found at any other site was from the thoracic mesothelium of a control male at the terminal sacrifice. Human cases of mesotheliomas are most frequent in the thoracic cavity. A recent report documented a total of only 11 human cases of scrotal meosthelioma (Japko et al., 1982).

The biological basis for the unique response of the scrotal mesothelium of Fischer 344 rats appears to be largely unknown. Although the data is not presented, Whitaker et al. (1982) note that clusters of cells in which the rate of cell division may be 10 times or more above the overall rate were most commonly noted in imprints of the testicular mesothelium. Mesotheliomas have been noted in several other bioassays using Fischer 344 rats. In the bioassay of cytembena (NTP, 1981) about two-thirds of the treated rats developed mesothelioma. Much lower tumor yields, on the order of those present in the rats given 2.0 or 0.5 mg acrylamide/kg/day in this study, were present in the bioassays of ethyl tellurac (NCI, 1979a), o-toluidine hydrochloride (NCI, 1979b) and ethylene oxide (Snellings et al., 1981).

The biological basis for the variety of tumors encountered in this study is unknown. Except for the benign mammary tumors, all the tumor types considered induced by acrylamide are uncommon with the historical background incidence

usually 3% or less. At the dose levels used in this study, there appears to be no preferential distribution of acrylamide to any of the affected organs (Miller et al., 1982; Ramsey et al., 1984). The above investigators have shown that excretion rate is not influenced by dose levels ranging from 0.05 to 100 mg/kg. Thus, an effect due to altered distribution or metabolism at the higher dose levels in this study (0.5 and 2.0 mg/kg/day) is unlikely.

Recent results with in vivo systems also suggest the oncogenic potential of acrylamide. Bull et al. (1984) used both a mouse skin initiation-promotion assay and a mouse lung adenoma assay. In the skin bioassay, mice were given total doses of 75, 150 or 300 mg acrylamide/kg by 6 applications over 2 weeks. The doses were applied either topically, by gastric intubation or by intraperitoneal injection. The mice were then treated with a promotor (TPA) for 20 weeks. All mice were sacrificed after one year. Acrylamide was found to induce increased incidence of skin tumors (both benign and malignant) at all tested dose levels and by all methods of application.

In the mouse lung bioassay, mice were given acrylamide 3 times per week for 8 weeks. Total gavage doses were 150, 300 or 600 mg/kg while intraperitoneal injection total doses varied from 24 to 1440 mg/kg. The mice were sacrificed after an additional 6 or 7 months. Although a positive dose-response relationship was reported, individual comparisons were not. Lung tumors appeared to be increased in mice given total doses of 72 mg/kg or more by injection and 150 mg/kg per os.

Under the conditions of this study, ingestion of acrylamide appears to induce a variety of neoplasms in Fischer 344 rats. The types of tumors induced are diverse and a unifying concept for their induction is unknown. With the exception of the scrotal meosthelioma, only rats given 2.0 mg/kg/day had significantly increased incidences of the tumor types previously presented. Scrotal meostheliomas occurred with increased incidence at doses of 0.1 mg/kg/day or more (statistically significant increases were present in the 0.5 and 2.0 mg/kg/day dose groups). The relevance of the unique response of the scrotal mesothelium of the Fischer 344 rat to risk assessment is unknown.

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K. A. Johnson, D.V.M., Ph.D.
Research Leader
Diplomate, American College of
Veterinary Pathologists

S. J. Gorzinski, M.S.
Research Leader
Study Director

K. M. Bodner, M.S.P.H.
Research Statistician

R. A. Campbell, B.S.
Analytical Chemist

Reviewed by:

M. J. McKenna, Ph.D.
Research Manager
Diplomate, American Board of
Toxicology

TITLE OF STUDY: ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

In compliance with Good Laboratory Practice Regulations, the study phases were inspected by the Quality Assurance Unit and the results of these inspections reported to Management and the Study Director on the dates listed below. The report accurately reflects the data generated in accordance with the regulations and standard operating procedures of the laboratory. All data and reports are located at the submitting laboratory.

Study Started:	15 Sept. 1980	Report Issued Date:	21 Sept. 1984
Dates of Inspection:	5 Sept. 1980	Date of Report:	5 Sept. 1980
	20 Oct. 1980		20 Oct. 1980
	11 Dec. 1980		12 Dec. 1980
	26 Jan. 1981		2 Feb. 1981
	16 Mar. 1981		17 Mar. 1981
	2 June 1981		12 June 1981
	17 June 1981		22 June 1981
	25 Aug. 1981		25 Aug. 1981
	28 Sept. 1981		6 Oct. 1981
	12 Oct. 1981		12 Oct. 1981
	1 Dec. 1981		3 Dec. 1981
	29 Dec. 1981		30 Dec. 1981
	8 Mar. 1982		8 Mar. 1982
	1 Apr. 1982		6 Apr. 1982
	25 May 1982		28 May 1982
	19 Aug. 1982		20 Aug. 1982
	3 Apr. 1984		3 Apr. 1984
	14 June 1984		19 June 1984

W. E. Hoover 9/21/84

W. E. Hoover — Date

Quality Assurance
Health & Environmental Sciences, USA
1803 Building
Dow Chemical U.S.A.
Midland, MI 48640

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FIGURE 1

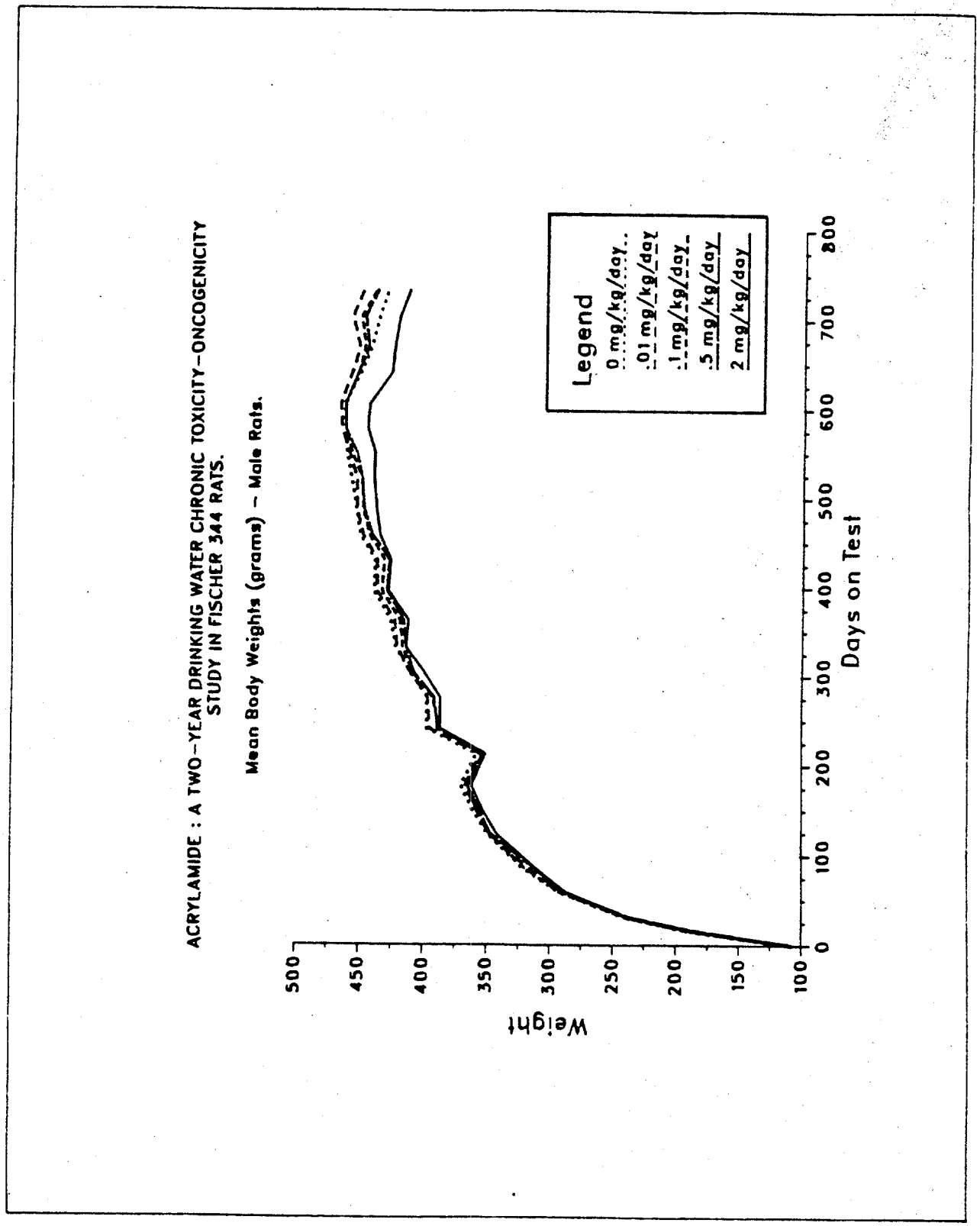
ACRYLAMIDE : A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS.
Mean Body Weights (grams) - Male Rats.
Weight
500
450
400
350
300
250
200
150
100
0
100
200
300
400
500
600
700
800
Days on Test
Legend
0 mg/kg/day
.01 mg/kg/day
.1 mg/kg/day
.5 mg/kg/day
2 mg/kg/day

FIGURE 2

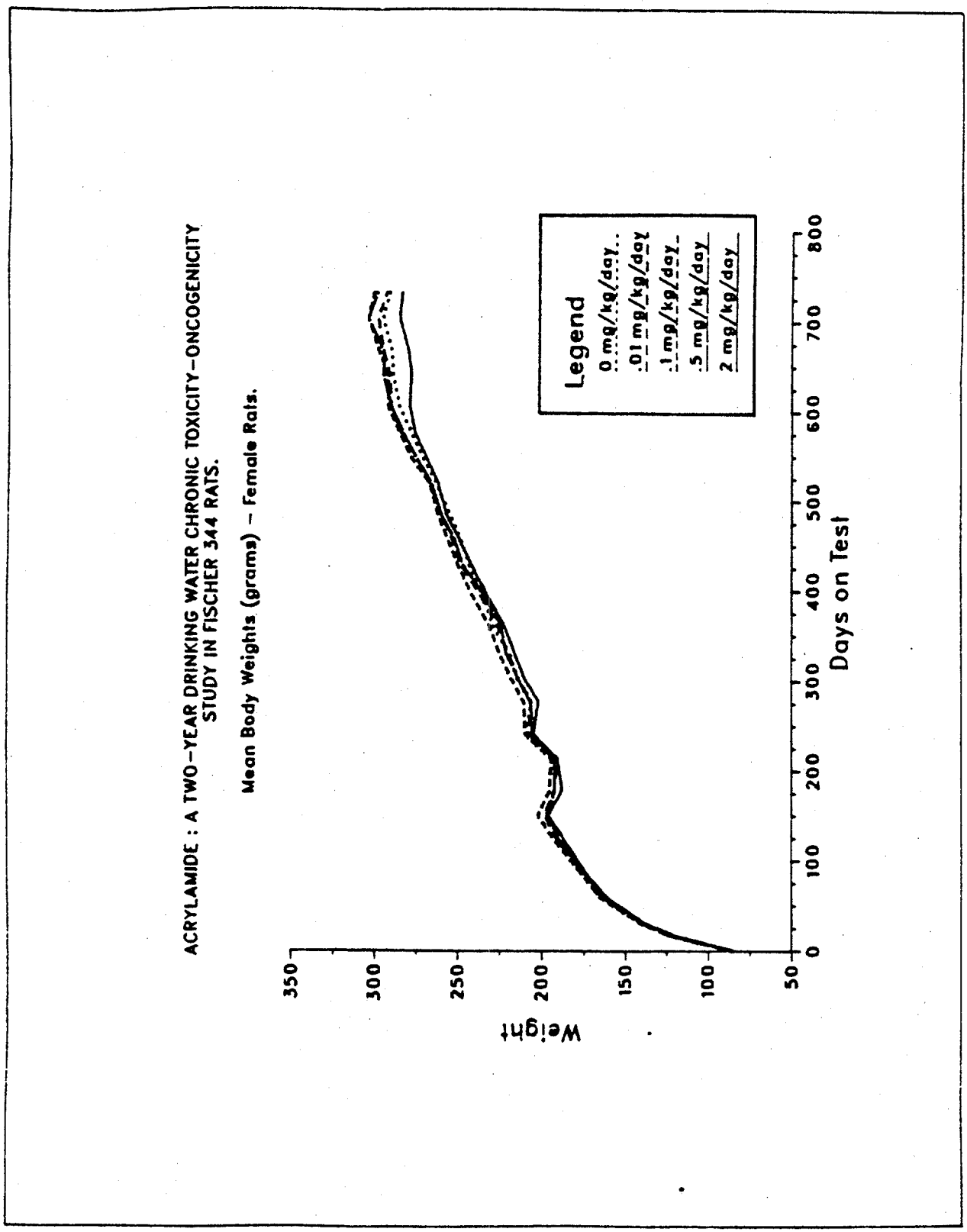
ACRYLAMIDE : A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS.
Mean Body Weights (grams) - Female Rats.
Weight
350
300
250
200
150
100
50
0
100
200
300
400
500
600
700
800
Days on Test
Legend
0 mg/kg/day
.01 mg/kg/day
.1 mg/kg/day
.5 mg/kg/day
2 mg/kg/day

FIGURE 3

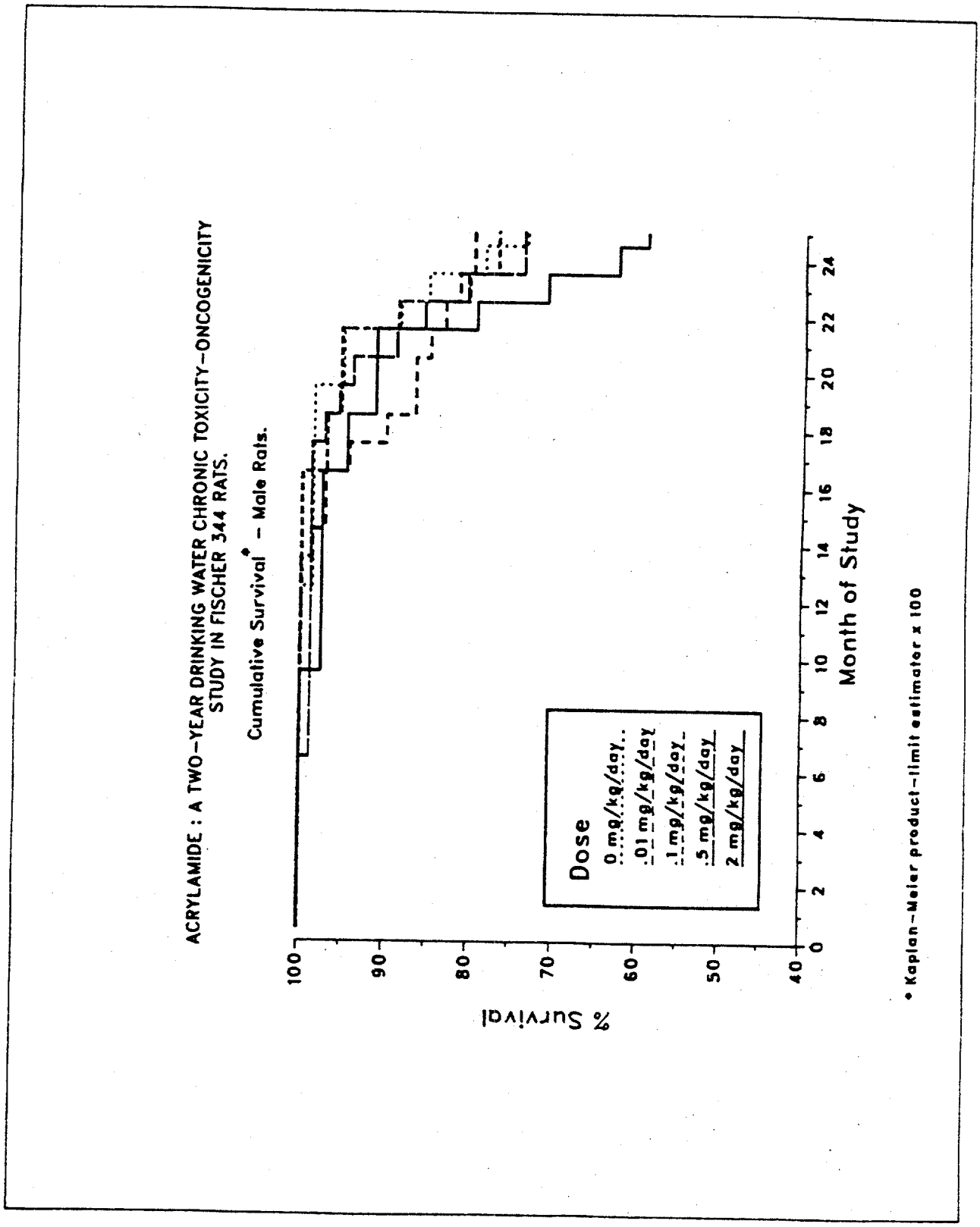
ACRYLAMIDE : A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS.
Cumulative Survival* - Male Rats.
% Survival
100
90
80
70
60
50
40
0
2
4
6
8
10
12
14
16
18
20
22
24
Month of Study
Dose
0 mg/kg/day
.01 mg/kg/day
.1 mg/kg/day
.5 mg/kg/day
2 mg/kg/day
* Kaplan-Meier product-limit estimator x 100

FIGURE 4

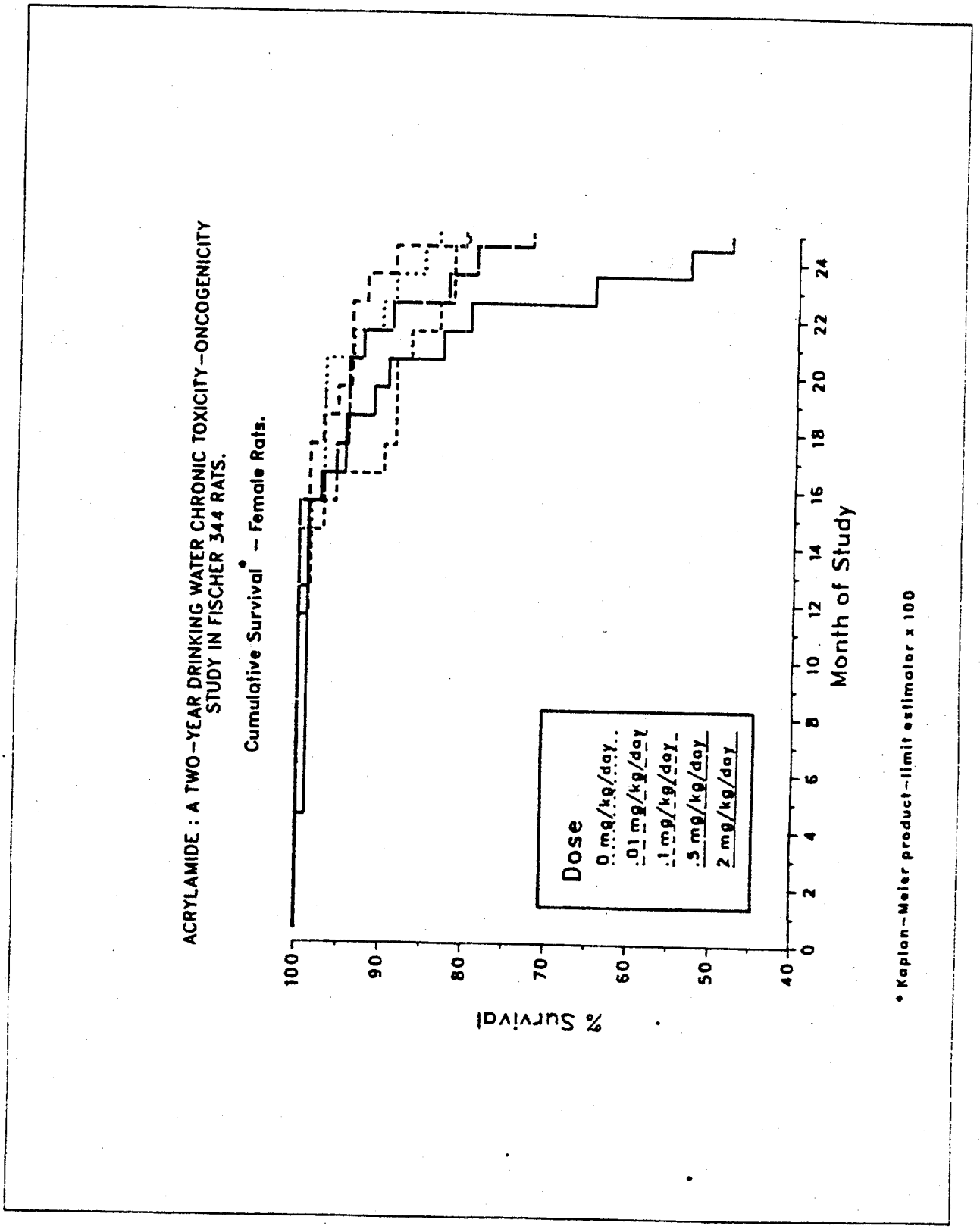
ACRYLAMIDE : A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS.
Cumulative Survival* - Female Rats.
% Survival
100
90
80
70
60
50
40
0
2
4
6
8
10
12
14
16
18
20
22
24
Month of Study
Dose
0 mg/kg/day
.01 mg/kg/day
.1 mg/kg/day
.5 mg/kg/day
2 mg/kg/day
* Kaplan-Meier product-limit estimator x 100

TABLE 1

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Analytical Results - Test Material[a]

	Sample Numbers				
	1	2	3	4	1[b]
Acrylic Acid	<1 ppm	NA	NA	NA	<1 ppm
Acetamide	<1 ppm	NA	NA	ND	<1 ppm
Methacrylonitrile	<1 ppm	NA	NA	ND	<1 ppm
Acrylonitrile	2.5 ppm	<1 ppm	<5 ppm	<10 ppm	<1 ppm
Ethylacetate	<1 ppm	3 ppm	<1 ppm	ND	<1 ppm
3 Hydroxypropionitrile	15 ppm	14 ppm	10-15 ppm[c]	<20 ppm	20 ppm
Soluble Polymer	600 ppm	230 ppm	4000 ppm	334 ppm	600 ppm
Insoluble Polymer[d]	2%	ND	NA	NA	NA
Water	0.4%	3.8%	1%	1%	0.5%
Purity by difference	97.5%	96.2%	98.6%	99.0%	-

[a]A new sample was recrystallized for each 6-month interval by W. N. Vanderkooi from monomer research, Dow Chemical Co., Midland, Michigan.

[b]One-year analyses results on the first (#1) recrystallized sample to assess possible changes in impurities, primarily water and acrylonitrile. Insoluble polymer was not analyzed, thus for this sample purity by difference could not be calculated.

[c]This value is an estimation due to incomplete chromatographic separation.

[d]Insoluble polymer removed by improved recrystallization method after first sample was processed. The water concentrate (premix) was filtered to remove the insoluble polymer before preparing the dosing solutions for the animals and thus not quantitated.

NA = Not Analyzed.
ND = Not Detected.

TABLE 2

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Summary of Drinking Water Analyses[a]

Sex	Dose (mg/kg/day) 0	0.01	0.1	0.5	2.0
Males	N.D.[b] (60)	94±9 (84)	96±10 (56)	96±4 (19)	96±5 (10)
Females	N.D.[b] (39)	95±8 (82)	95±8 (42)	105±3 (3)	100±3 (3)

[a]Values are mean±S.D. of the percent of target mg/kg/day dose level for the number of samples indicated in the parentheses. Samples were analyzed after being accessible to the rats for 4 days. Three samples [one 0.1 mg male (3% of targeted) and two 0.1 mg female (each 10.8% of targeted)] were omitted from calculations.

[b]N.D. = Not detected. Limit of detection of 0.02-0.05 ppm and 0.06-1 ppm for 87 and 12 samples, respectively.

TABLE 3

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Tissues Collected During Gross Necropsy Examination

adrenal glands
aorta
auditory sebaceous (Zymbal) glands
bone
bone marrow
brain
cecum
cervix
coagulating glands
epididymides
esophagus
eyes
heart
kidneys
lacrimal glands
large intestine
larynx
liver
lungs
mammary gland
mediastinal lymph node
mediastinal tissue
mesenteric lymph node
mesenteric tissue
nasal turbinates
ovaries
oviducts
pancreas
parathyroid glands
peripheral nerve
pituitary
prostate
salivary glands
seminal vesicles
skeletal muscle
skin
small intestine
spinal cord
spleen
stomach
testes
thymus
thyroid gland
tongue
trachea
urinary bladder
uterus
vagina
gross lesions

TABLE 4

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Mean Body Weights (Grams)[a] - Males

Days on Test	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
0[b]	108± 7	108± 8	108± 7	106± 7	106± 7
3[b]	124± 8	121± 9	122± 6	119± 8	121± 7
10[b]	157±10	155±13	154±10	148±11	154±10
17[b]	194±14	191±14	192±13	189±13*	190±13
24[b]	220±14	216±15	217±12	212±14	218±11
31[b]	238±14	238±13	240±13	236±14	237±12
38[b]	251±17	249±17	254±14	247±13	249±13
45[b]	266±17	263±17	267±15	262±13	265±10
52[b]	279±19	276±18	279±15	271±14	276± 9
59[b]	292±18	289±15	292±15	289±15	287±11
66[b]	300±19	297±20	297±12	294±14	293±15
73[b]	308±18	306±20	306±13	304±15	302±16
80[b,c]	316±19	313±22	313±12	312±14	307± 7
87	322±19	317±22	319±18	313±14	309±17
89[b]	324±18	321±15	323±15	320±17	317±14*
94[b]	332±14	329±22	327±12	325±14	322±17
122	348±20	349±23	343±12	343±14	338±16
124	349±20	348±17	348±15	347±17	342±15*
150	361±20	358±17	358±17	356±16	353±16*
178	370±22	367±19	365±17	365±19	362±17*
213	358±26	355±21	353±21	353±23	351±24
241	397±21	395±19	388±16*	389±19*	387±18*
276	397±23	397±20	393±17	392±19	387±19*
304	411±25	411±20	409±17	408±19	400±17*
332	422±26	421±21	417±17	414±18*	414±20*
362	426±25	423±21	419±18	416±19*	412±18*
395	439±26	437±22	433±18	429±10*	428±21*
430	438±28	437±22	431±19	427±21*	426±19*
458	450±28	448±21	443±19	441±21	435±21*
486	453±30	453±22	448±20	447±20	438±22*
521	457±30	453±21	449±22	449±22	440±21*
549	461±31	459±26	457±26	453±22	439±28*
577	462±33	465±23	462±27	462±29	445±21*
605	463±33	466±24	462±28	462±26	443±21*
640	450±36	457±25	452±35	452±24	426±27*
668	442±34	451±25	447±36	444±23	424±29*
703	436±37	457±25*	450±37	447±24	420±26*
733	429±40	448±25*	438±30	437±26	412±23*

[a]Values are mean body weight±S.D. for all rats alive at time of weighing (up to 90/group).

[b]Values are mean body weight±S.D. for a subgroup of 20 rats/sex/group.

[c]Although all rats were scheduled to be weighed on this day, values are for the subgroup of 20 rats/sex/group due to a problem with the weighing pan. Statistical analysis of differences was not performed on these data; therefore, the animals were reweighed on day 89.

*Statistically identified difference from control by Dunnett's test, α=0.05.

TABLE 5

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Mean Body Weights (Grams)[a] - Females

Days on Test	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
0[b]	85± 5	85± 5	86± 5	85± 5±	85± 5
3[b]	92± 4	92± 4	95± 5	94± 8	95± 5
10[b]	108± 6	109± 6	111± 6	112± 7	109± 4
17[b]	124± 7	122± 7	123± 7	121± 8*	121± 7*
24[b]	132± 6	133± 7	137± 6	133± 5	131± 4
31[b]	140± 8	140± 8	141± 7	140± 9	139± 7
38[b]	146± 8	147± 8	149± 8	145± 5	147± 8
45[b]	155± 8	153± 8	159± 7	155± 9	154± 9
52[b]	158± 9	157± 8	162± 8	160± 9	158± 9
59[b]	165± 9	163± 8	165± 9	163±10	161±10
66[b]	168± 8	168± 8	171± 9	168±12	169±10
73[b]	172± 9	173± 9	176± 9	173±10	174±11
80[b]	176± 9	176± 9	180± 8	177±11	178±12
87[b]	176±10	175±10	177± 9	175±10	174±10
94[b]	180± 8	180± 5	184± 7	182±10	181±12
122	191± 8	191± 9	196± 9	191± 9	188±11
124	191±10	191± 9	193±10	190±10	187±10*
150	197±10	198± 9	202±11*	197±10	196±11
178	192±11	192±10	195±11	192±10	188±12*
213	191±13	190±11	194±13	193±14	191±13
241	209±11	207±10	210±12	206±11	205±12
276	206±11	206± 9	211±12*	207±12	202±12
304	215±12	215±11	219±13	215±13	211±12
332	220±14	221±11	226±15*	222±14	217±13
362	230±15	227±11	232±17	225±15	223±14*
395	235±16	237±15	242±18*	235±17	233±14
430	244±19	249±19	251±20	248±22	243±16
458	249±18	254±20	257±21*	253±21	250±18
486	256±20	261±21	263±21	261±21	258±17
521	264±19	268±20	268±22	267±21	263±18
549	272±19	276±22	279±23	276±21	270±17
577	279±20	285±21	286±19	284±21	277±17
605	286±20	291±21	293±20	291±23	280±20
640	290±19	292±19	293±20	296±23	279±25*
668	291±19	296±19	299±22	296±27	281±31
703	296±21	299±19	305±21	305±20	286±36
733	291±24	293±26	301±24	299±29	284±28

[a]Values are mean body weight±S.D. for all rats alive at time of weighing (up to 90/group).

[b]Values are mean body weight±S.D. for a subgroup of 20 rats/sex/group.

*Statistically identified difference from control by Dunnett's test, α=0.05.

TABLE 6

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Water Consumption[a] - Males

Days on Test	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
1-3	18.9± 1.2	19.4± 1.4	20.2± 1.4	19.8± 1.3	19.4± 0.6
4-7	19.5± 1.2	20.2± 6.0	20.5± 1.3	19.5± 1.1	20.2± 0.8
8-10	24.0± 1.4	23.6± 2.4	24.4± 1.5	24.0± 2.2	23.6± 1.0
11-14	23.3± 1.3	23.7± 2.4	23.6± 1.4	22.6± 2.7	22.9± 0.9
15-17	24.3± 1.3	25.9± 2.9	25.2± 1.7	23.8± 1.6	23.8± 1.1
18-21	23.8± 1.1	25.2± 2.3	24.5± 1.4	23.2± 0.7	24.0± 1.3
22-24	24.6± 0.9	26.5± 1.2	24.6± 1.1	23.6± 1.0	25.7± 1.1
25-28	24.3± 0.4	26.8± 2.9	24.6± 1.1	23.7± 0.4	24.6± 1.1
29-31	24.7± 1.0	27.1± 2.2	25.5± 1.5	24.0± 0.8	25.7± 0.7
32-35	23.8± 1.1	25.7± 2.1	25.6± 1.9	23.1± 0.5	24.6± 0.7
36-38	25.4± 2.0	26.8± 1.9	26.1± 1.3	24.1± 0.8	25.1± 1.0
39-42	24.9± 1.6	25.7± 1.0	25.8± 1.6	23.5± 1.1	24.8± 1.4
43-45	26.6± 1.7	27.6± 2.2	27.6± 1.5	25.3± 1.1	26.1± 1.4
46-49	24.6± 1.5	25.3± 1.6	25.9± 1.1	23.7± 1.0	24.3± 0.8
50-52	26.1± 1.2	25.8± 2.0	26.4± 0.8	23.7± 1.0	26.6± 1.1
53-56	25.0± 0.7	25.3± 1.3	25.8± 1.0	24.1± 0.9	24.7± 1.2
57-59	23.9± 0.6	25.3± 1.2	25.6± 0.7	23.2± 0.5	25.1± 1.6
60-63	22.2± 0.8	23.1± 1.5	23.3± 0.8	23.3± 4.1	22.1± 1.5
64-66	22.6± 0.6	23.8± 1.6	24.7± 1.4	23.2± 0.9	22.6± 1.0
67-70	23.5± 1.0	23.2± 1.4	23.4± 1.4	23.4± 1.8	22.9± 1.9
71-73	23.2± 0.7	25.0± 2.1	26.0± 1.5	23.7± 1.0	23.7± 1.2
74-77	22.0± 1.4	24.0± 1.5	23.3± 1.0	21.9± 0.8	22.4± 0.9
78-80	22.6± 0.6	23.4± 1.0	24.1± 0.8	23.2± 0.9	24.4± 6.1
81-84	22.5± 1.0	23.0± 1.6	22.6± 1.0	21.4± 1.0	22.3± 0.6
85-87	23.8± 1.2	23.9± 1.1	25.0± 0.9	23.6± 0.5	24.1± 0.9
88-91	23.5± 1.2	23.7± 1.3	23.7± 0.8	23.4± 0.9	23.8± 0.9
92-94	23.4± 1.0	24.2± 1.4	25.1± 0.4	23.6± 0.6	25.2± 1.1
116-119	25.0± 3.5	25.0± 1.0	24.9± 1.5	23.4± 2.2	23.3± 3.4
120-122	23.6± 1.1	24.3± 1.6	24.8± 1.2	24.0± 1.1	23.0± 1.0
144-147	22.7± 0.8	22.5± 1.5	24.2± 0.7	22.0± 1.0	21.2± 2.7
148-150	23.6± 1.1	24.1± 1.5	25.5± 1.3	24.3± 0.9	26.1± 1.9
172-175	23.0± 1.0	24.3± 1.5	24.2± 1.1	22.4± 0.7	21.7± 3.3
176-178	23.5± 0.4	24.1± 1.8	24.8± 1.2	24.0± 3.2	23.3± 0.9
207-210	17.3± 1.9	17.9± 2.5	17.0± 2.2	18.4± 3.7	18.1± 2.4
211-213	26.9± 7.3	26.4± 5.8	22.3± 4.1	25.7± 4.6	25.5± 9.8

[a]Values are mean water consumption (g/rat/day) ±S.D. for a subgroup of 19-21 animals.

Statistical analyses are not reported.

TABLE 6 (Continued)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Water Consumption[a] - Males

Days on Test	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
235-238	22.0± 1.6	21.7± 1.5	21.3± 1.0	20.3± 1.3	22.4± 1.5
239-241	22.0± 1.3	22.8± 1.6	22.4± 1.2	21.6± 1.4	23.5± 1.8
270-273	17.8± 1.8	17.7± 1.5	17.1± 1.2	16.4± 0.9	17.4± 2.3
274-276	21.0± 1.0	22.3± 1.7	21.2± 0.8	19.9± 1.4	22.6± 2.7
298-301	21.0± 0.9	20.9± 1.5	20.4± 0.7	20.4± 1.2	20.8± 1.2
302-304	21.9± 1.5	22.7± 1.5	22.1± 1.3	21.7± 0.5	22.7± 1.3
326-329	20.7± 1.6	20.7± 1.5	20.2± 0.7	18.2± 0.2	20.2± 1.1
330-332	21.8± 1.8	22.3± 2.0	21.7± 1.4	20.6± 0.9	21.5± 0.9
361-364	20.8± 1.5	21.3± 0.9	21.0± 1.3	20.2± 0.9	21.1± 0.8
365-367	21.9± 2.5	22.0± 1.8	21.6± 0.8	20.3± 2.1	21.8± 1.9
368-392	23.5± 1.2	22.7± 1.7	22.8± 1.3	22.4± 1.7	23.4± 1.4
393-395	23.2± 1.7	23.8± 1.5	23.3± 1.7	22.9± 1.9	25.3± 1.6
424-427	22.0± 1.4	22.6± 1.7	21.9± 1.5	21.2± 1.4	23.2± 0.8
452-455	21.6± 1.4	21.0± 2.3	21.5± 1.0	21.2± 1.6	21.5± 1.2
456-458	24.6± 1.6	24.3± 0.9	23.6± 1.7	23.9± 2.5	23.8± 2.5
480-483	23.4± 1.7	24.5± 1.5	23.9± 1.4	24.2± 2.5	25.0± 1.7
484-486	23.9± 2.2	25.0± 2.0	24.1± 1.7	25.0± 2.8	25.7± 2.8
512-514	23.5± 1.6	24.3± 2.1	23.1± 0.8	23.7± 1.9	25.3± 2.0
515-518	22.5± 3.3	24.0± 2.0	21.9± 0.8	22.7± 2.2	23.0± 2.1
519-521	24.6± 1.9	25.3± 1.9	24.6± 1.7	25.0± 2.5	25.7± 2.3
543-546	22.9± 1.8	23.6± 1.7	23.1± 2.0	22.3± 1.6	23.6± 1.6
547-549	24.4± 2.4	26.6± 1.9	25.8± 2.3	25.0± 2.4	25.3± 2.0
571-574	23.3± 1.4	22.7± 2.3	22.7± 1.1	21.9± 2.2	24.8± 2.6
575-577	24.9± 1.6	26.2± 3.9	25.4± 1.9	24.1± 2.3	26.0± 1.7
599-602	23.9± 2.4	23.9± 2.2	23.2± 1.1	22.3± 1.6	25.0± 3.2
603-605	25.2± 2.6	24.0± 0.6	25.4± 2.2	24.6± 2.8	27.2± 2.8
641-644	23.1± 2.9	23.7± 2.1	25.3± 2.8	22.7± 5.1	25.5± 2.0
645-647	25.1± 3.7	25.3± 1.5	27.0± 3.6	25.8± 3.6	26.3± 2.7
662-665	24.9± 3.2	24.3± 5.7	24.9± 4.1	24.1± 4.5	26.4± 3.5
666-668	26.3± 2.8	26.4± 6.7	25.4± 3.1	25.8± 4.0	26.6± 2.6
697-700	24.1± 2.0	25.2± 2.2	25.3± 3.7	25.3± 2.8	24.9± 2.1
701-703	26.2± 2.0	26.6± 2.4	26.7± 3.0	26.4± 2.9	26.7± 3.3

[a]Values are mean water consumption (g/rat/day) ±S.D. for a subgroup of 19-21 animals.

Statistical analyses are not reported.

TABLE 7

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Water Consumption[a] - Females

Days on Test	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
1-3	16.0± 1.0	16.2± 0.8	17.1± 0.6	17.5± 1.0	17.0± 0.4
4-7	16.2± 0.9	16.6± 1.2	17.6± 0.8	18.0± 1.2	17.3± 0.5
8-10	19.3± 1.5	18.6± 0.9	20.9± 1.0	21.1± 1.2	21.0± 1.2
11-14	17.5± 0.9	17.0± 1.1	19.0± 0.9	19.4± 1.1	18.4± 0.8
15-17	19.1± 1.4	17.7± 0.9	19.2± 1.5	19.4± 1.4	20.1± 2.6
18-21	19.4± 4.8	19.2± 3.6	22.6± 5.1	20.7± 1.5	21.2± 7.5
22-24	19.4± 1.1	18.3± 1.2	19.6± 1.0	20.8± 1.8	19.0± 1.0
25-28	18.3± 0.4	18.1± 1.3	19.3± 0.9	19.2± 1.5	18.6± 4.7
29-31	18.7± 1.5	18.0± 0.7	19.9± 1.1	19.8± 1.3	18.9± 0.6
32-35	17.2± 1.1	17.4± 1.0	18.3± 1.4	18.2± 1.3	17.8± 1.1
36-38	18.8± 1.5	18.2± 1.2	20.3± 1.1	19.9± 0.8	19.3± 1.1
39-42	17.6± 0.8	17.5± 1.2	19.0± 1.1	19.4± 1.6	18.4± 1.1
43-45	19.7± 1.0	19.3± 1.3	20.2± 1.1	20.1± 1.6	20.3± 1.2
46-49	17.9± 0.9	17.9± 1.1	19.2± 1.3	18.8± 0.8	19.3± 1.4
50-52	20.6± 1.1	20.2± 4.6	19.9± 1.1	20.7± 2.0	20.5± 1.7
53-56	17.9± 1.7	18.7± 1.7	18.5± 1.1	19.7± 2.0	18.8± 2.0
57-59	18.3± 1.0	19.0± 2.0	19.3± 1.3	19.3± 1.1	21.4± 2.1
60-63	16.0± 1.1	17.1± 2.2	16.8± 1.8	17.6± 1.3	17.9± 1.1
64-66	17.5± 1.6	18.2± 1.0	18.9± 1.5	19.7± 2.0	18.9± 1.8
67-70	17.1± 0.9	16.7± 0.9	17.7± 1.2	18.2± 1.2	18.0± 1.3
71-73	18.0± 2.3	18.3± 1.2	18.8± 1.0	18.9± 0.9	19.7± 1.5
74-77	17.5± 1.4	17.0± 1.3	17.2± 0.9	21.0± 5.2	18.0± 1.4
78-80	17.9± 1.0	19.1± 1.3	19.9± 1.1	19.4± 1.1	21.3± 2.8
81-84	16.7± 1.1	16.7± 1.1	17.5± 1.0	18.1± 1.3	18.1± 0.9
85-87	19.1± 1.2	20.1± 1.3	20.1± 1.8	19.2± 1.3	20.7± 1.1
88-91	17.6± 1.0	18.2± 2.0	18.2± 0.8	18.1± 3.4	24.9±10.5
92-94	18.3± 0.9	19.5± 1.3	20.1± 1.5	19.8± 1.1	20.0± 1.5
116-119	18.9± 2.1	18.1± 1.0	19.6± 0.7	18.4± 2.3	18.1± 1.0
120-122	18.6± 0.5	18.3± 0.6	19.8± 1.1	19.3± 1.4	18.7± 5.7
144-147	17.3± 1.5	16.2± 1.0	17.9± 1.4	16.4± 1.2	16.2± 1.1
148-150	19.1± 1.7	19.4± 0.7	20.5± 0.8	19.0± 0.9	18.9± 1.9
172-175	15.6± 1.4	14.4± 0.9	15.5± 2.3	15.7± 0.8	15.5± 1.2
176-178	21.6± 1.7	20.7± 2.1	21.2± 1.8	23.0± 2.4	20.4± 0.7
207-210	15.6± 2.0	15.2± 6.2	16.0± 2.4	17.8± 2.1	16.1± 1.3
211-213	28.3±10.9	17.5± 1.6	27.2±10.8	18.8± 2.2	20.6± 5.2

[a]Values are mean water consumption (g/rat/day) ± S.D. for a subgroup of 19-21 animals.

Statistical analyses are not reported.

TABLE 7 (Continued)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Water Consumption[a] - Females

Days on Test	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
235-238	15.4± 3.5	16.4± 1.8	17.0± 1.2	17.9± 3.1	16.5± 2.0
239-241	18.0± 2.5	17.3± 1.3	19.1± 0.6	20.3± 2.3	17.1± 1.1
270-273	14.9± 1.8	15.1± 1.6	14.9± 1.0	16.1± 3.2	14.9± 1.1
274-276	18.0± 6.8	16.9± 1.6	16.8± 1.3	18.1± 5.7	16.2± 0.6
298-301	17.1± 1.5	16.6± 1.3	18.0± 1.5	18.0± 2.8	17.3± 0.8
302-304	18.1± 2.1	16.9± 1.0	18.4± 0.9	19.7± 3.0	18.5± 1.8
326-329	16.1± 4.0	16.6± 2.6	16.5± 1.2	18.6± 4.5	17.3± 2.3
330-332	17.1± 1.8	17.1± 1.2	19.4± 1.7	17.0± 0.7	17.9± 1.4
361-364	17.5± 1.7	16.4± 1.7	19.1± 2.6	17.1± 2.7	18.0± 1.8
365-367	18.4± 1.8	16.8± 1.1	18.7± 1.6	20.1± 3.2	18.9± 2.0
389-392	19.9± 2.5	19.0± 1.8	20.6± 1.7	20.9± 2.5	20.6± 2.1
393-395	18.9± 1.2	20.3± 2.0	21.3± 1.8	21.2± 2.9	20.8± 1.9
424-427	17.7± 2.2	18.3± 2.3	18.2± 2.0	19.3± 3.1	20.5± 4.5
452-455	16.4± 0.8	16.9± 1.6	18.4± 1.2	17.5± 1.2	19.5± 2.1
456-458	19.1± 2.0	19.5± 1.7	19.7± 0.5	20.6± 2.8	23.2± 5.4
480-483	17.9± 5.0	18.5± 2.6	19.3± 2.4	20.2± 3.1	20.9± 2.5
484-486	20.3± 3.0	20.6± 2.8	20.5± 2.5	21.9± 3.2	22.8± 2.5
512-514	20.8± 2.1	22.8± 3.4	21.5± 2.4	23.8± 2.9	21.6± 5.1
515-518	20.4± 2.4	19.4± 2.5	20.4± 1.4	20.7± 2.0	20.1± 4.9
519-521	20.6± 3.5	20.6± 2.1	22.8± 2.6	24.7± 3.5	24.1± 3.0
543-546	18.3± 1.8	20.3± 3.1	22.2± 2.1	22.3± 2.3	22.6± 4.7
547-549	21.1± 2.9	22.2± 2.4	24.4± 3.1	24.8± 2.7	24.2± 3.6
571-574	20.9± 4.1	21.0± 2.1	22.3± 2.3	22.4± 2.8	22.1± 2.7
575-577	23.1± 3.5	24.2± 3.0	25.2± 3.1	25.4± 6.4	25.6± 4.5
599-602	20.2± 1.7	21.0± 2.9	21.6± 2.3	23.9± 4.0	23.0± 4.3
603-605	24.8± 6.0	23.2± 2.7	24.3± 3.5	26.2± 5.9	23.3± 3.3
641-644	21.6± 3.6	21.2± 3.3	22.9± 3.6	21.8± 1.4	25.8± 6.2
645-647	21.5± 3.2	23.2± 3.2	27.2± 5.5	24.7± 2.9	24.5± 2.5
662-665	20.5± 3.1	21.6± 3.4	24.1± 4.3	23.0± 5.3	24.8± 4.1
666-668	23.4± 3.4	23.4± 3.5	25.8± 3.7	24.8± 6.6	25.9± 3.2
697-700	24.3± 4.7	24.3± 4.8	24.1±12.1	27.2± 5.2	27.2± 9.1
701-703	24.1± 3.9	25.5± 4.9	27.9± 6.9	27.3± 4.5	29.4± 9.1

[a]Values are mean water consumption (g/rat/day) ±S.D. for a subgroup of 19-21 animals.

Statistical analyses are not reported.

TABLE 8

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Food Consumption[a] - Males

Days on Test	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
1-8	15.4± 1.0	15.1± 0.8	15.4± 0.5	14.8± 0.9	15.4± 0.5
9-15	16.9± 1.1	16.5± 1.2	17.1± 0.8	16.1± 0.8	17.0± 0.4
16-22	17.9± 0.9	17.7± 1.0	18.3± 0.7	17.4± 0.9	18.3± 0.5
23-29	17.5± 0.8	17.3± 0.9	18.1± 0.6	17.3± 0.6	18.4± 0.2
30-36	17.4± 0.7	17.6± 0.4	18.0± 0.5	16.8± 0.6	17.6± 0.4
37-43	17.3± 0.8	17.5± 0.6	18.0± 0.7	17.2± 0.5	17.7± 0.5
44-50	17.1± 0.8	16.8± 0.9	17.8± 0.7	17.0± 0.6	17.4± 0.5
51-57	16.9± 0.7	16.5± 0.6	17.5± 0.7	16.3± 0.5	18.2± 0.5
58-64	16.3± 0.4	16.3± 0.8	16.8± 0.5	16.3± 0.8	17.1± 0.4
65-71	16.7± 0.6	16.1± 0.6	16.4± 0.7	16.2± 0.6	16.4± 0.4
72-78	16.3± 0.7	16.2± 2.2	16.7± 0.3	16.5± 0.5	16.3± 0.6
79-85	16.0± 0.7	15.7± 0.7	15.8± 0.3	15.2± 0.4	16.4± 0.5
86-92	16.7± 0.8	16.3± 0.9	16.8± 0.3	15.9± 0.4	16.9± 0.5
121-127	16.8± 1.2	16.6± 1.2	16.9± 0.4	16.2± 0.9	17.2± 0.7
149-155	17.0± 0.7	16.2± 1.3	17.3± 0.6	16.0± 0.5	17.7± 1.0
177-183	16.6± 1.0	15.6± 0.9	15.7± 0.3	16.0± 0.2	15.8± 0.6
233-239	15.8± 1.4	16.4± 0.8	16.2± 1.1	15.5± 0.7	17.3± 1.1
240-246	15.8± 0.8	15.7± 1.1	15.4± 0.8	15.0± 0.8	16.2± 0.9
275-281	16.7± 0.8	16.5± 0.8	16.6± 0.3	16.2± 0.6	16.8± 1.1
303-309	16.9± 0.9	16.7± 0.8	16.8± 0.8	16.2± 0.7	17.5± 0.7
331-337	17.2± 0.8	17.1± 1.1	17.0± 1.0	16.4± 0.8	17.6± 0.7
352-358	17.2± 1.0	17.3± 0.8	17.5± 0.6	16.7± 0.6	17.9± 0.7
394-400	17.8± 1.0	17.2± 0.7	17.0± 0.8	17.0± 0.8	18.2± 0.7
429-435	17.8± 0.9	17.6± 0.9	17.2± 0.8	17.1± 0.9	18.0± 0.8
457-463	18.1± 0.9	17.7± 1.0	17.9± 1.1	17.7± 1.0	18.8± 0.9
485-491	17.5± 1.0	17.2± 0.7	17.4± 0.9	17.5± 0.8	18.2± 1.1
520-526	17.4± 0.8	17.8± 0.7	17.9± 1.2	17.1± 1.3	18.1± 1.0
562-568	17.8± 1.4	17.5± 1.1	17.7± 0.9	17.1± 1.1	17.8± 0.8
576-582	17.7± 0.9	17.9± 1.5	17.6± 0.9	17.1± 0.7	17.5± 1.2
604-610	17.2± 1.0	17.2± 1.5	17.4± 1.1	16.8± 0.7	18.3± 1.2
639-645	17.1± 1.8	18.1± 1.3	18.1± 1.6	17.9± 1.4	18.5± 1.7
667-673	17.5± 1.5	18.1± 1.2	16.7± 4.0	17.5± 1.2	18.0± 1.0
702-708	17.1± 2.4	18.0± 1.6	17.6± 1.9	18.7± 1.6	18.1± 1.1

[a]Values are mean food consumption (g/rat/day) ±S.D. for a subgroup of 16-21 animals.

Statistical analyses are not reported.

TABLE 9

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Food Consumption[a] - Females

Days on Test	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
1-8	11.5± 0.4	11.6± 0.6	12.1± 0.4	12.4± 0.9	12.1± 0.4
9-15	11.7± 0.5	11.5± 0.5	12.0± 0.4	12.2± 0.6	12.5± 0.4
16-22	11.9± 0.8	11.6± 0.5	12.1± 0.4	12.3± 0.7	12.1± 0.4
30-36	11.2± 1.0	11.1± 0.7	11.8± 0.4	11.7± 0.5	12.2± 0.6
37-43	11.6± 0.6	11.0± 0.3	12.0± 0.6	11.3± 0.4	12.3± 0.7
44-50	11.6± 0.4	11.0± 0.4	12.3± 1.4	11.4± 0.6	11.6± 0.5
51-57	11.6± 0.8	11.5± 0.4	11.6± 0.5	11.7± 0.9	11.6± 1.4
58-64	11.0± 0.9	11.1± 0.6	11.4± 0.5	11.4± 0.4	11.8± 0.4
65-71	11.1± 0.8	10.7± 0.4	11.4± 0.6	11.1± 0.3	11.4± 0.5
72-78	11.3± 0.9	11.0± 0.7	12.5± 1.4	11.4± 0.3	12.3± 1.1
79-85	11.2± 0.7	11.2± 0.9	11.8± 0.4	12.0± 1.0	11.3± 0.5
86-92	11.3± 0.7	11.2± 0.4	11.9± 0.5	11.6± 0.6	11.8± 0.7
121-127	11.6± 0.5	11.2± 0.6	12.2± 0.7	11.6± 0.7	12.2± 1.0
149-155	11.4± 0.6	10.9± 0.4	11.7± 0.6	10.9± 0.5	11.1± 0.5
177-183	13.0± 0.5	11.3± 0.9	12.4± 0.4	12.5± 0.3	12.3± 1.0
233-239	10.1± 0.5	9.9± 0.9	10.1± 0.4	10.3± 0.7	10.5± 0.3
240-246	9.9± 0.7	9.7± 0.6	10.8± 0.8	10.7± 0.9	10.3± 0.7
275-281	10.2± 1.6	11.5± 1.0	11.1± 0.6	11.0± 0.8	11.6± 1.4
303-309	11.4± 0.8	11.3± 0.9	11.7± 0.6	11.9± 1.1	11.8± 0.7
331-337	12.0± 0.9	12.3± 1.2	12.1± 0.7	12.0± 0.7	12.5± 0.7
352-358	12.1± 0.7	11.8± 0.9	11.8± 0.8	11.6± 0.7	12.0± 0.3
394-400	12.6± 0.6	13.2± 2.0	13.0± 0.7	12.7± 0.6	12.7± 0.6
429-435	12.4± 1.0	12.8± 0.9	13.5± 1.2	13.1± 0.6	13.7± 1.0
457-463	12.9± 0.7	13.2± 0.7	13.4± 0.9	13.2± 0.9	13.7± 0.8
485-491	13.2± 0.7	13.1± 1.0	12.4± 1.5	13.2± 0.8	13.6± 0.9
520-526	12.8± 1.1	12.9± 0.9	13.6± 0.1	13.5± 0.8	14.1± 0.8
562-568	13.1± 1.1	13.9± 1.0	13.8± 0.7	13.2± 1.0	13.3± 1.2
576-582	13.5± 1.0	13.7± 1.0	13.5± 0.4	13.5± 1.0	13.2± 1.1
604-610	13.8± 1.1	13.9± 1.1	14.3± 0.9	13.8± 0.7	13.4± 1.6
639-645	14.4± 1.4	14.6± 1.3	14.5± 0.7	13.9± 1.1	14.5± 1.3
667-673	13.9± 0.7	14.4± 1.2	14.8± 1.4	13.3± 2.3	13.6± 1.5
702-708	13.3± 1.6	14.4± 0.9	13.7± 1.6	13.7± 1.8	14.1± 1.7

[a]Values are mean food consumption (g/rat/day) ±S.D. for a subgroup of 16-21 animals.

Statistical analyses are not reported.

TABLE 10

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Palpable Mass Observations - Males

Dose (mg/kg/day)	Animal Number	Observation	Date Observed[a] initial date - final date	Final Disposition[b]
0	80A-3155	enlarged testicles - abdomen bloated	23 June 82 - 27 July 82	H - Mesothelioma.
	80A-3159	sore and swollen area - hind leg	23 June 82 - 28 July 82	G - Not present.
	80A-3162	growth - side	25 Aug. 82 - 24 Sept. 82	H - Osteogenic sarcoma of rib.
	80A-3163	mass - side	23 June 82 - 24 Sept. 82	H - Mammary fibroma - side.
		swollen foot	23 June 82 - 24 Sept. 82	G - Trauma - foot.
	80A-3164	mass - thorax	28 July 82 - 24 Sept. 82	H - Mammary fibroadenoma.
	80A-3166	growth - thorax	25 Aug. 82 - 24 Sept. 82	H - Mammary fibroma.
		sore - scrotum	28 July 82 - 24 Sept. 82	G - Scrotal sore not present.
	80A-3178	mass - lip	22 Jan. 81 - 24 Feb. 81	P - Mass on lip no longer apparent on 24 Feb. 81.
	80A-3184	sore - foot	26 Jan. 82 - 23 Feb. 82	P - Sore on rear foot disappeared on 23 Feb. 82.
	80A-3187	scab - ear tag	22 July 81 - 19 Aug. 81	P - Ear noted as okay on 19 Aug. 81.
	80A-3191	mass protruding from anus	28 July 82 - 28 Sept. 82	H - Polypoid ademona of large intestine.
	80A-3197	mass - side	28 July 82 - 22 Sept. 82	H - Skin - fibrosarcoma.
	80A-3198	mass - preputial	26 May 82 - 23 June 82	H - Skin - undifferentiated sarcoma.
	80A-3209	scabby sore - foot	28 July 82 - 28 Sept. 82	G - Rear foot ulcer.
	80A-3218	growth - side	25 Aug. 82 - 22 Sept. 82	H - Keratoacanthoma of skin.
	80A-3223	eye bulging	23 June 82 - 30 June 82	H - Inflammation of cornea and lacrimal gland.
	80A-3224	growth - flank	22 July 81 - 29 Sept. 81	H - Inflammation of preputial gland.
0.01	80A-3250	mass axillary	28 July 82 - 24 Sept. 82	H - Mammary fibroadenoma.
	80A-3264	wart on nose	26 May 82 - 24 Sept. 82	G - Not present.
	80A-3266	growth near apex of left eye	18 Feb. 82 - 11 Mar. 82	H - Lacrimal gland - undifferentiated carcinoma.
	80A-3268	growth - flank	22 July 81 - 2 Oct. 81	P - Growth disappeared 2 Oct. 81.
	80A-3269	growth - flank	2 Oct. 81 - 30 Oct. 81	P - Growth disappeared 30 Oct. 81.
	80A-3270	growth - forearm	26 May 82 - 22 July 82	H - Skin - squamous papilloma.
	80A-3290	mass - axillary	28 July 82 - 28 Sept. 82	H - Mammary fibroma.
	80A-3291	growth - flank	2 Oct. 81 - 30 Oct. 81	P - Growth disappeared 30 Oct. 81.
	80A-3303	mass - axillary	23 June 82 - 28 Sept. 82	H - Mammary fibroma.
		mass on ear	28 July 82 - 25 Aug. 82	P - Mass on ear gone 25 Aug. 82.
	80A-3306	enlarged testicle	23 June 82 - 30 Sept. 82	H - Testicle - Leydig cell tumor.
	80A-3308	growth - flank	19 Aug. 81 - 2 Oct. 81	P - Growth disappeared 2 Oct. 81.
	80A-3309	growth - rear caudal area	2 Oct. 81 - 26 Jan. 82	P - Growth disappeared 26 Jan. 82.
		mass - perianal	28 July 82 - 30 Sept. 82	H - Skin - fibrosarcoma.
	80A-3316	enlarged eye	20 Apr. 82 - 30 Sept. 82	H - Increased vascularity, cornea.
		mass - preputial	26 May 82 - 23 June 82	P - Mass gone 23 June 82.

[a] Initial date is the date the observation was first recorded on the palpable mass sheet. Final date is either the date of necropsy of the rat or the date the observation was noted as having regressed.

[b] G means the final disposition was at gross necropsy. P refers to palpable mass sheet and H means the final disposition was at histopathologic exam.

TABLE 10 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Palpable Mass Observations - Males

Dose (mg/kg/day)	Animal Number	Observation	Date Observed[a] initial date - final date	Final Disposition[b]
0.1	80A-3326	growth - back	2 Oct. 81 - 24 Sept. 82	H - Skin - keratoacanthoma.
	80A-3327	sore - shoulder	20 Apr. 82 - 22 Sept. 82	H - Skin - basal cell adenoma.
	80A-3328	enlarged testicles	26 May 82 - 20 July 82	H - Leydig cell tumor of testes and mesothelioma of tunic.
	80A-3330	mass - preputial	20 Apr. 82 - 23 June 82	P - Mass gone on 23 June 82.
	80A-3334	mass - dorsal side	26 May 82 - 14 Sept. 82	H - Skin - fibroma.
		mass - prefemoral	28 July 82 - 14 Sept. 82	H - Mammary - 3 tumors (one fibroadenoma and two fibromas).
		mass - axillary	28 July 82 - 14 Sept. 82	
	80A-3341	mass - side	26 May 82 - 26 July 82	H - Mammary - fibroma.
	80A-3342	mass - preputial	20 Apr. 82 - 24 Sept. 82	H - Skin - carcinoma.
		testicle - enlarged	26 May 82 - 24 Sept. 82	H - Testes - Leydig cell tumor.
	80A-3348	mass - inguinal	23 June 82 - 24 Sept. 82	H - Mammary - fibroma.
	80A-3352	growth - abdomen	24 June 81 - 22 July 81	P - Growth disappeared 22 July 81.
	80A-3358	mass - side	26 May 82 - 20 Sept. 82	H - Mammary - fibroma.
	80A-3361	mass - pinna of ear	30 Dec. 81 - 24 Sept. 82	H - Skin (pinna of ear) - fibroma.
	80A-3364	growth - lip	30 Dec. 81 - 26 Jan. 82	P - Lip growth disappeared 26 Jan. 82
		mass - axillary	23 June 82 - 22 Sept. 82	H - Mammary - fibroma.
	80A-3368	mass - shoulder	26 Jan. 82 - 28 Sept. 82	H - Skin - lipoma.
	80A-3376	growth - flank	22 July 81 - 2 Oct. 81	P - Growth disappeared 2 Oct. 81.
	80A-3378	rear foot paralyzed	12 Jan. 82 - 10 Feb. 82	H - Tibia - osteogenic sarcoma of rear leg.
	80A-3382	growth - preputial	23 Feb. 82 - 20 Apr. 82	P - Growth disappeared 20 Apr. 82.
				G - Scab 28 Sept. 82.
				H - Skin - inflammation of subcutis.
	80A-3386	mass - shoulder	26 Jan. 82 - 28 Sept. 82	H - Skin - lipoma.
	80A-3388	mass - dorsal side	23 Mar. 82 - 8 July 82	H - Mammary - fibroma.
	80A-3396	mass - head	23 June 82 - 9 July 82	H - Auditory sebaceous (Zymbal) gland - carcinoma.
	80A-3401	enlarged testicles	28 July 82 - 30 Sept. 82	H - Testes - Leydig cell tumor and mesothelioma of tunic.
	80A-3406	mass - shoulder	28 July 82 - 30 Sept. 82	H - Skin - basal cell adenoma.

[a] Initial date is the date the observation was first recorded on the palpable mass sheet. Final date is either the date of necropsy of the rat or the date the observation was noted as having regressed.

[b] G means the final disposition was at gross necropsy. P refers to palpable mass sheet and H means the final disposition was at histopathologic exam.

TABLE 10 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Palpable Mass Observations - Males

Dose (mg/kg/day)	Animal Number	Observation	Date Observed[a] initial date - final date	Final Disposition[b]
0.5	80A-3417	mass - back	23 Feb. 82 - 22 Sept. 82	G - Not present.
	80A-3425	cyst - axillary	23 June 82 - 24 Sept. 82	H - Mammary - fibroadenoma.
	80A-3435	growth - penis	26 May 82 - 24 Sept. 82	H - Prepuce - squamous papilloma.
		mass - axillary	23 June 82 - 24 Sept. 82	H - Mammary - fibroadenoma.
	80A-3438	growth - lip	20 Apr. 82 - 3 May 82	H - Lip - abscess.
	80A-3443	mass - shoulder	26 May 82 - 7 June 82	H - Skin - epidermal inclusion cyst.
	80A-3447	mass - hip	23 Feb. 82 - 21 July 82	H - Mammary - fibroma.
		mass - side	26 May 82 - 21 July 82	H - Mammary - fibroma.
	80A-3454	mass - eyelid	23 June 82 - 22 Sept. 82	G - Verrucous thickening of eyelid, not found in wet tissues.
	80A-3455	mass - rectal/scrotal	2 Oct. 81 - 24 Sept. 82	H - Skin - fibrosarcoma.
	80A-3456	mass - ear area	28 July 82 - 24 Sept. 82	H - Pinna - myxoma.
	80A-3463	ear tag - sore	30 Dec. 81 - 26 Jan. 82	P - Swelling gone on 26 Jan. 82.
	80A-3468	cyst - shoulder	23 June 82 - 28 Sept. 82	H - Skin - keratoacanthoma.
	80A-3477	mass - axillary	23 June 82 - 28 June 82	H - Mammary - fibroma.
		bloated abdomen	23 June 82 - 28 June 82	H - Abdominal cavity - mesothelioma.
	80A-3485	growth - flank	19 Aug. 81 - 2 Oct. 81	H - Preputial gland impaction.
		growth - eyelid	20 Apr. 82 - 28 Sept. 82	H - Skin - fibroma on eyelid.
	80A-3491	wart on nose	28 July 82 - 28 Sept. 82	H - Skin - epithelial hyperplasia.
	80A-3493	mass - axillary	26 May 82 - 10 June 82	G - Not recognized.
	80A-3494	enlarged testicles	23 June 82 - 13 Sept. 82	H - Leydig cell tumor - testes, mesothelioma, tunic.
	80A-3499	mass - shoulder	26 Jan. 82 - 30 Sept. 82	H - Mammary - fibroma.
		ear tag - sore	20 Apr. 82 - 30 Sept. 82	G - Ear tag sore not present.

[a] Initial date is the date the observation was first recorded on the palpable mass sheet. Final date is either the date of necropsy of the rat or the date the observation was noted as having regressed.

[b] G means the final disposition was at gross necropsy. P refers to palpable mass sheet and H means the final disposition was at histopathologic exam.

TABLE 10 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Palpable Mass Observations - Males

Dose (mg/kg/day)	Animal Number	Observation	Date Observed[a] initial date - final date	Final Disposition[b]
2.0	80A-3519	growth - side	25 Aug. 82 - 24 Sept. 82	H - Mammary - fibroma.
	80A-3520	growth - dorsal hip	26 May 82 - 24 Sept. 82	H - Skin - sebaceous adenoma.
		mass - axillary	28 July 82 - 24 Sept. 82	H - Mammary - fibroma.
	80A-3524	mass - hip	20 Apr. 82 - 21 June 82	H - Mammary - fibroma.
	80A-3529	mass - ear	23 June 82 - 28 July 82	H - Auditory sebaceous (Zymbal) gland - carcinoma.
	80A-3530	growth - preputial	30 Oct. 81 - 30 Dec. 81	P - Growth disappeared 30 Dec. 81.
		mass - side	20 Apr. 82 - 20 Sept. 82	H - Skin - keratoacanthoma.
	80A-3531	growth - nose	23 June 82 - 24 Sept. 82	H - Skin - squamous papilloma.
	80A-3535	growth - back	2 Oct. 81 - 23 Feb. 82	P - Growth disappeared 23 Feb. 82.
		growth - near ear	20 Apr. 82 - 21 June 82	H - Auditory sebaceous (Zymbal) gland - carcinoma.
	80A-3536	enlarged testicles	28 July 82 - 10 Aug. 82	H - Testes - Leydig cell tumor.
	80A-3538	scars - tail	23 Feb. 82 - 19 Mar. 82	G - Tail - scabs and scales.
	80A-3543	growth - preputial	30 Oct. 81 - 23 Feb. 82	P - Growth disappeared 23 Feb. 82.
		mass - back	26 May 82 - 14 Sept. 82	H - Skin - sebaceous adenoma.
		mass - axillary	23 June 82 - 14 Sept. 82	H - Mammary - fibroma.
	80A-3544	growth - hip	26 Jan. 82 - 20 Apr. 82	P - Growth disappeared 20 Apr. 82.
	80A-3554	growth - rear foot	23 June 82 - 22 Sept. 82	G - Abscess.
	80A-3555	growth - flank	19 Aug. 81 - 2 Oct 81	P - Growth gone 2 Oct. 81.
	80A-3558	mass - axillary	23 June 82 - 24 Sept. 82	H - Skin - lipoma.
	80A-3559	growth - flank	22 July 81 - 19 Aug. 81	P - Growth disappeared 19 Aug. 81.
	80A-3562	bloated abdomen	23 June 82 - 9 July 82	H - Leukemia of multiple organs.
	80A-3568	mass - axillary	26 May 82 - 12 Aug. 82	H - Mammary - fibroma.
		mass - hip	26 May 82 - 12 Aug. 82	H - Mammary - fibroma.
		mass - prefemoral	28 July 82 - 12 Aug. 82	H - Mammary - fibroma.
	80A-3570	mass - shoulder	26 May 82 - 23 June 82	H - Mammary - fibroma.
	80A-3572	abscess - preputial	26 Jan. 82 - 23 Feb. 82	P - Abscess disappeared 23 Feb. 82.
		mass - preputial	26 May 82 - 20 Aug. 82	H - Preputial gland - inflammation.
	80A-3579	sore - hind foot	30 Dec. 81 - 26 Jan. 82	P - Sore healed 26 Jan. 82.
	80A-3582	enlarged testicles	20 Apr. 82 - 26 July 82	G - Ulcer, 22 Sept. 82.
	80A-3584	enlarged eye	30 Dec. 81 - 28 Sept. 82	H - Testes - Leydig cell tumor and tunic - mesothelioma.
		mass - axillary	28 July 82 - 28 Sept. 82	H - Cataract of eye.
	80A-3586	growth - ventral side	26 Jan. 82 - 24 Aug. 82	H - Mammary - fibroadenoma.
	80A-3594	mass - axillary	28 July 82 - 28 Sept. 82	H - Preputial gland - carcinoma.
				H - Mammary - galactocele.

[a] Initial date is the date the observation was first recorded on the palpable mass sheet. Final date is either the date of necropsy of the rat or the date the observation was noted as having regressed.

[b] G means the final disposition was at gross necropsy. P refers to palpable mass sheet and H means the final disposition was at histopathologic exam.

TABLE 11

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Palpable Mass Observations - Females

Dose (mg/kg/day)	Animal Number	Observation	Date Observed[a] initial date - final date	Final Disposition[b]
0	80A-3689	growth - nose	26 May 82 - 4 June 82	H - Skin - squamous papilloma.
	80A-3691	mass - side	26 May 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3701	mass - side	26 May 82 - 27 Sept. 82	H - Mammary adenocarcinoma and a fibroadenoma.
		mass - inguinal	30 July 82 - 27 Sept. 82	
	80A-3718	mass - lower jaw	21 Apr. 81 - 25 Nov. 81	H - Ameloblasticodontoma of tooth.
	80A-3724	mass - axillary	30 July 82 - 23 Sept. 82	H - Mammary fibroadenoma.
	80A-3736	growth - both axillary areas	27 Aug. 82 - 20 Sept. 82	H - Skin - basal cell adenoma and mammary - fibroadenoma.
	80A-3740	mass - head	23 June 82 - 29 Sept. 82	H - Skin - epidermal inclusion cyst.
	80A-3742	mass - axillary	23 June 82 - 29 Sept. 82	H - Mammary adenocarcinoma and fibroadenoma.
		mass - inguinal	30 July 82 - 29 Sept. 82	
	80A-3750	mass - axillary	30 July 82 - 30 Sept. 82	H - Mammary fibroadenoma.
	80A-3760	mass - hip	26 May 82 - 14 June 82	H - Skin - epidermal inclusion cyst.
	80A-3769	mass - axillary	23 June 82 - 30 Sept. 82	H - Two mammary fibroadenomas and one galactocele.
		mass - inguinal	27 Aug. 82 - 30 Sept. 82	
0.01	80A-3776	mass - side	20 Apr. 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3783	mass - axillary	30 July 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3792	mass - axillary	26 May 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3801	mass - side	26 Jan. 82 - 27 Sept. 82	H - Skin - basal cell adenoma.
	80A-3803	mass - lip	23 June 82 - 27 Sept. 82	H - Skin - squamous papilloma of lip.
	80A-3805	mass - protruding from vagina	30 July 82 - 10 Aug. 82	H - Stromal cell sarcoma-of cervix.
	80A-3806	mass - side	26 Jan. 82 - 27 Sept. 82	H - Mammary adenoma and fibro-adenoma.
	80A-3814	mass - axillary	26 May 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3817	mass - axillary	30 July 82 - 24 Aug. 82	H - Mammary fibroadenoma.
	80A-3822	mass - axillary	26 May 82 - 29 Sept. 82	H - Mammary fibroadenoma.
	80A-3847	mass - axillary	27 Aug. 82 - 29 Sept. 82	H - Mammary fibroadenoma.
	80A-3859	wart - eyelid	26 May 82 - 30 Sept. 82	H - Fibrous histiocytoma of the skin (eyelid).

[a] Initial date is the date the observation was first recorded on the palpable mass sheet. Final date is either the date of necropsy of the rat or the date the observation was noted as having regressed.

[b] G means the final disposition was at gross necropsy. P refers to palpable mass sheet and H means the final disposition was at histopathologic exam.

TABLE 11 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Palpable Mass Observations - Females

Dose (mg/kg/day)	Animal Number	Observation	Date Observed[a] initial date - final date	Final Disposition[b]
0.1	80A-3873	mass - inguinal	26 May 82 - 20 July 82	H - Clitoral gland adenoma.
	80A-3874	mass - axillary	30 July 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3877	mass - inguinal	26 Jan. 82 - 16 Feb. 82	H - Clitoral gland adenoma.
	80A-3889	mass - cervical	23 June 82 - 23 Sept. 82	H - Mammary fibroadenoma.
	80A-3891	mass - cervical	26 May 82 - 23 Sept. 82	H - Mammary fibroadenoma.
	80A-3900	enlarged eye	2 Oct. 81 - 23 Sept. 82	H - Eye - increased vascularity of the cornea and anterior synechia of the iris.
	80A-3921	mass - side	26 May 82 - 29 Sept. 82	H - Mammary adenocarcinoma.
	80A-3922	mass - nose	26 May 82 - 23 Sept. 82	H - Skin - squamous papilloma of nose (external nares).
	80A-3930	mass - inguinal	26 May 82 - 30 July 82	P - Mass noted to be gone on 30 July 82. G - Mass was noted 29 Sept. 82. H - Normal subcutaneous tissue with 2 lymph nodes present.
	80A-3934	mass - flank	23 Feb. 82 - 29 Sept. 82	H - Mammary fibroadenoma.
	80A-3936	mass - axillary	20 Apr. 82 - 29 Sept. 82	H - Mammary fibroadenoma.
	80A-3950	mass - side	27 Aug. 82 - 30 Sept. 82	G - Not present.
	80A-3955	mass - side	26 May 82 - 30 Sept. 82	H - Mammary fibroadenoma.
0.5	80A-3960	mass - inguinal	30 July 82 - 1 Sept. 82	H - Histiocytic sarcoma of multiple organs (metastases).
	80A-3961	mass - inguinal	23 June 82 - 27 Sept. 82	H - Clitoral gland adenoma.
	80A-3964	mass - axillary	23 June 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3969	mass - inguinal	23 June 82 - 20 Sept. 82	H - Mammary fibroadenoma.
	80A-3976	mass - inguinal	26 Jan. 82 - 23 Sept. 82	H - Clitoral gland adenocarcinoma.
	80A-3977	mass - axillary	26 May 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3983	mass - side	26 May 82 - 22 Sept. 82	H - Mammary adenoma and fibroadenoma.
	80A-3992	mass - axillary	26 Jan. 82 - 27 Sept. 82	H - Two mammary fibroadenomas.
	80A-3994	mass - cervical	23 June 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3995	mass - axillary	23 June 82 - 27 Sept. 82	H - Mammary fibroadenoma.
	80A-3999	mass - jaw	26 May 82 - 30 July 82	H - Skin (jaw area) - squamous cell carcinoma.
	80A-4001	mass - inguinal	30 July 82 - 29 Sept. 82	H - Clitoral gland adenoma.
	80A-4003	mass - axillary	30 July 82 - 29 Sept. 82	H - Mammary - galactocele.
	80A-4011	mass - axillary	23 Feb 82 - 2 July 82	H - Two mammary fibroadenomas.
	80A-4034	mass - preputial	30 Dec. 81 - 3 Sept. 82	H - Clitoral gland adenocarcinoma and four mammary fibroadenomas.
		mass - axillary	23 June 82 - 3 Sept. 82	
		mass - axillary	23 June 82 - 3 Sept. 82	
	80A-4035	mass - inguinal	23 June 82 - 23 Sept. 82	H - Inguinal mass was a mammary fibroadenoma.
		mass - side	27 Aug. 82 - 23 Sept. 82	G - Mass on side not present.
	80A-4038	mass - inguinal	26 May 82 - 10 Aug. 82	H - Mammary fibroadenoma.

[a] Initial date is the date the observation was first recorded on the palpable mass sheet. Final date is either the date of necropsy of the rat or the date the observation was noted as having regressed.

[b] G means the final disposition was at gross necropsy. P refers to palpable mass sheet and H means the final disposition was at histopathologic exam.

TABLE 11 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Palpable Mass Observations - Females

Dose (mg/kg/day)	Animal Number	Observation	Date Observed[a] initial date - final date	Final Disposition[b]
2.0	80A-4046	mass - inguinal	30 Dec. 81 - 27 Sept. 82	H - Clitoral gland adenoma.
	80A-4058	growth - inguinal	30 Dec. 81 - 19 Jan. 82	H - Mammary fibroadenoma.
	80A-4063	mass - axillary	30 July 82 - 19 Aug. 82	H - Mammary fibroadenoma and a galactocele.
	80A-4064	mass - axillary	30 July 82 - 23 Sept. 82	H - Mammary fibroadenoma and two galactoceles.
	80A-4065	mass - axillary	30 July 82 - 27 Sept. 82	H - Mammary fibroadenoma and a galactocele.
	80A-4069	mass - inguinal	23 June 82 - 17 Sept. 82	H - Clitoral gland adenoma.
	80A-4070	mass - abdomen	30 July 82 - 27 Aug. 82	H - Mammary fibroma.
	80A-4075	sore - preputial	20 Apr. 82 - 19 July 82	H - Clitoral gland adenoma.
	80A-4076	mass - abdomen	23 Mar. 82 - 21 Sept. 82	H - Mammary adenoma.
	80A-4077	mass - head	20 Apr. 82 - 11 June 82	H - Auditory sebaceous (Zymbal) gland carcinoma.
	80A-4080	mass - axillary	23 June 82 - 26 July 82	H - Mammary adenocarcinoma.
	80A-4083	mass - side	26 May 82 - 23 Sept. 82	H - Three mammary fibroadenomas.
		mass - axillary	30 July 82 - 23 Sept. 82	
		mass - axillary	30 July 82 - 23 Sept. 82	
	80A-4084	mass - cervical	30 July 82 - 23 Sept. 82	H - Mammary fibroadenoma.
	80A-4088	mass - side	20 Apr. 82 - 20 Aug. 82	H - Mammary fibroadenoma.
	80A-4091	mass - axillary	30 July 82 - 23 Sept. 82	H - Two mammary fibroadenomas.
	80A-4107	mass - side	26 May 82 - 23 Sept. 82	H - Mammary fibroadenoma.
	80A-4115	mass - shoulder	23 Feb. 82 - 10 Sept. 82	H - Mammary fibroma.
	80A-4118	mass - shoulder	30 Dec. 81 - 8 Jan. 82	H - Mammary fibroma.
	80A-4120	mass - axillary	27 Aug. 82 - 29 Sept. 82	H - Mammary fibroadenoma.
	80A-4125	enlarged eye	26 May 82 - 30 July 82	H - Inflammation of the cornea. G - Exophthalmia of eye seen on gross exam caused by squamous cell carcinoma in oral cavity.
	80A-4127	mass - rear	23 Mar. 82 - 5 May 82	H - Mammary adenocarcinoma.
	80A-4129	mass - abdomen	23 Mar. 82 - 29 Sept. 82	H - Mammary fibroma.
	80A-4133	mass - hindquarter	23 Mar. 82 - 30 Aug. 82	H - Mammary fibroma.
	80A-4135	mass - axillary	23 June 82 - 29 Sept. 82	H - Mammary fibroadenoma.

[a] Initial date is the date the observation was first recorded on the palpable mass sheet. Final date is either the date of necropsy of the rat or the date the observation was noted as having regressed.

[b] G means the final disposition was at gross necropsy. P refers to palpable mass sheet and H means the final disposition was at histopathologic exam.

TABLE 12

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Cumulative Mortality[a]

Sex	Males					Females				
Dose (mg/kg/day)	0.0	0.01	0.1	0.5	2.0	0.0	0.01	0.1	0.5	2.0
Number of Rats in Group	60	60	60	60	60	60	60	60	60	61
Months on Test										
1	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	1
7	0	0	0	1	0	0	0	0	0	1
8	0	0	0	1	0	0	0	0	0	1
9	0	0	0	1	0	0	0	0	0	1
10	0	0	0	1	2	0	0	0	0	1
11	0	0	0	1	2	0	0	0	0	1
12	0	0	0	1	2	0	1	0	0	1
13	1	0	0	1	2	0	1	1	0	1
14	1	1	0	1	2	0	1	1	0	1
15	1	2	0	1	2	1	1	2	0	1
16	1	2	0	1	2	2	1	3	2	2
17	1	4	2	1	4	2	1	7	3	4
18	1	7	2	2	4	2	2	8	4	4
19	1	9	3	3	6	2	3	8	4	6
20	3	9	3	4	6	2	4	8	4	7
21	3	10	3	7	6	4	4	9	5	11
22	7	11	7	9	12	6	4	11	7	13
23	9	12	12	12	18	7	5	12	11	22
24	13	13	14	16	23	9	7	12	13	29
24 to termination	16	13	14	16	25	10	12	13	17	32
Total	16	13	14	16	25*	10	12	13	17	32*

[a]Data presented as number of rats dead at each monthly interval.

*Statistically different from control group by Gehan-Wilcoxon test, $\alpha = 0.05$.

TABLE 13

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Hematologic Examination[a] - Males at Terminal Sacrifice

Dose (mg/kg/day)	Number of Samples	RBC$_6$ x 10^6/ cu mm	Hgb (gm/dl)	PCV (%)	MCV cu mi	MCH uug	MCHC (%)	Plat$_3$ x 10^3/ cu mm	WBC$^b_3$ x 10^3/ cu mm	Differential Count (%) Seg	Lym	Mono	Eos	NRBC/ 100 WBC
0	10	8.42 ±0.89	17.1 ±1.8	47.4 ±4.5	56. ±2.	20.3 ±0.5	36.1 ±0.7	876. ±139.	8.4 ±1.7	43. ±7.	52. ±7.	4. ±3.	1. ±1.	3.[c] ±2.
0.01	10	8.53 ±0.88	17.1 ±1.6	47.2 ±4.5	55. ±1.	20.0 ±0.4	36.2 ±0.4	888. ±102.	6.6 ±1.4	-	-	-	-	-
0.1	10	7.63 ±1.67	16.0 ±2.5	44.1 ±7.6	59. ±4.	21.2 ±1.5	36.3 ±0.7	898. ±184.	7.4 ±2.3	-	-	-	-	-
0.5	10	8.14 ±0.92	16.6 ±1.5	46.3 ±4.3	57. ±1.	20.4 ±0.7	35.9 ±0.7	871. ±121.	5.8 ±1.4	-	-	-	-	-
2.0	10	7.47 ±1.06	15.5 ±2.1	42.5 ±6.0	57. ±1.	20.8 ±0.5	36.5 ±0.5	942. ±179.	8.7 ±4.7	46. ±7.	48. ±8.	5. ±3.	1. ±1.	3.[d] ±2.

[a] All data presented as mean±S.D. Statistical analyses are not reported.

[b] White blood cell counts were not corrected for nucleated RBC values.

[c] Examination of stained blood smears disclosed 5 rats with 1+ erythrocyte poikilocytosis and 3 rats with 1+ erythrocyte anisocytosis.

[d] Examination of stained blood smears disclosed 3 rats with 1+ erythrocyte poikilocytosis, 3 rats with 1+ erythrocyte anisocytosis, and 1 rat with 2+ poikilocytosis and 1+ polychromasia.

- Indicates no data.

TABLE 14

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Hematologic Examination[a] - Females at Terminal Sacrifice

Dose (mg/kg/day)	Number of Samples	RBC_6 x 10^6/ cu mm	Hgb (gm/dl)	PCV (%)	MCV cu mi	MCH uug	MCHC (%)	$Plat_3$ x 10^3/ cu mm	WBC^b_3 x 10^3/ cu mm	Differential Count (%) Seg	Lym	Mono	Eos	NRBC/ 100 WBC
0	10	7.07 ±1.04	15.4 ±1.7	41.6 ±4.8	59. ±4.	21.9 ±1.5	37.0 ±0.5	733. ±173.	5.1 ±1.8	41. ±8.	53. ±8.	5. ±3.	2. ±1.	7.[c] ±9.
0.01	10	7.20 ±1.05	15.7 ±1.6	42.6 ±4.0	60. ±4.	22.0 ±1.6	36.8 ±0.8	614. ±161.	15.5 ±35.3	-	-	-	-	-
0.1	10	6.90 ±1.80	15.0 ±3.0	40.7 ±8.9	61. ±7.	22.5 ±3.4	37.1 ±1.1	677. ±151.	6.4 ±4.1	-	-	-	-	-
0.5	10	7.32 ±0.56	15.6 ±1.1	42.4 ±2.9	58. ±1.	21.4 ±0.6	36.8 ±0.7	799. ±168.	4.4 ±0.6	-	-	-	-	-
2.0	10	5.38 ±2.06	11.9 ±4.3	31.9 ±11.7	60. ±10.	22.6 ±4.5	37.3 ±1.3	649. ±224.	13.2 ±21.4	52. ±13.	40. ±14.	7. ±5.	1. ±1.	19.[d] ±38.

[a]All data presented as mean±S.D. Statistical analyses are not reported.

[b]White blood cell counts were not corrected for nucleated RBC values.

[c]Examination of stained blood smears disclosed 1 rat with 1+ erythrocyte anisocytosis; 1 rat with 1+ anisocytosis and 1+ polychromasia; and 1 rat with 1+ anisocytosis and 2+ polychromasia.

[d]Examination of stained blood smears disclosed 1 rat with 1+ anisocytosis; 1 rat with 2+ anisocytosis; 1 rat with 1+ anisocytosis and 1+ polychromasia; 1 rat with 1+ anisocytosis and 2+ polychromasia; 1 rat with 2+ anisocytosis, 3+ polychomasia, 3+ hypochromia, and 1+ Howell-Jolly Bodies; and 1 rat with 3+ anisocytosis, 3+ polychromasia, and 1+ Howell-Jolly Bodies.

- Indicates no data.

TABLE 15

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Clinical Chemistry Values[a] - Males at Terminal Sacrifice

Dose (mg/kg/day)	Number of Samples	BUN (mg/dl)	SGPT (mU/ml)	AP (mU/ml)	GLUC (mg/dl)	TP (g/dl)	ALB (g/dl)	GLOB (g/dl)	CHE ($U \times 10^{-1}$/ml)
0	10	16. ±3.	48. ±15.	41. ±15.	127. ±11.	5.9 ±0.6	2.8 ±0.3	3.1 ±0.4	23.6 ±6.6
0.01	10	15. ±2.	44. ±18.	41. ±4.	155. ±10.	6.0 ±0.2	2.8 ±0.1	3.2 ±0.1	21.5 ±3.6
0.1	10	17. ±2.	40. ±7.	43. ±11.	138. ±20.	5.7 ±0.2	2.6 ±0.2	3.1 ±0.2	21.8 ±2.2
0.5	10	15. ±3.	40. ±9.	49. ±8.	139. ±31.	5.8 ±0.3	2.8 ±0.2	3.0 ±0.2	22.5 ±3.5
2.0	10	17. ±4.	50. ±20.	68. ±25.	133. ±12.	5.7 ±0.5	2.6 ±0.3	3.1 ±0.3	19.6 ±6.3

[a]Data presented as mean±S.D. Statistical analyses are not reported.

TABLE 16

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Clinical Chemistry Values[a] - Females at Terminal Sacrifice

Dose (mg/kg/day)	Number of Samples	BUN (mg/dl)	SGPT (mU/ml)	AP (mU/ml)	GLUC (mg/dl)	TP (g/dl)	ALB (g/dl)	GLOB (g/dl)	CHE ($U \times 10^{-1}$/ml)
0	8	14. ±4.	61. ±16.	46. ±18.	132. ±25.	6.7 ±0.4	3.4 ±0.1	3.3 ±0.4	39.9 ±12.1
0.01	10	13. ±1.	61. ±26.	39. ±13.	149. ±32.	6.5 ±0.3	3.4 ±0.2	3.1 ±0.2	39.9 ±4.0
0.1	10	14. ±4.	70. ±36.	50. ±31.	132. ±15.	6.3 ±0.3	3.3 ±0.2	3.0 ±0.3	36.1 ±10.2
0.5	10	14. ±1.	58. ±18.	39. ±20.	132. ±23.	6.3 ±0.5	3.2 ±0.3	3.1 ±0.4	38.6 ±5.4
2.0	10	18. ±7.	110. ±81.	81. ±57.	123. ±15.	5.5 ±1.0	2.8 ±0.5	2.7 ±0.6	24.4 ±12.5

[a]Data presented as mean±S.D. Statistical analyses are not reported.

TABLE 17

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Urinalysis[a] - Males at Terminal Sacrifice

	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
Specific Gravity	1.050 ±0.010	1.049 ±0.009	1.047 ±0.012	1.048 ±0.007	1.044 ±0.013
pH	7.0(6) 7.5(3)	7.0(5) 7.5(1) 8.0(3) 9.0(1)	6.0(1) 7.0(7) 8.0(2)	7.0(3) 7.5(2) 8.0(5)	6.0(1) 7.0(8) 8.0(1)
Protein	Trace (1) 2+(3) 3+(5)	1+(1) 2+(4) 3+(5)	2+(1) 3+(9)	2+(4) 3+(6)	2+(4) 3+(6)
Glucose	-(8) 1+(1)	-(9) 1+(1)	-(10)	-(10)	-(10)
Ketones	-(8)	-(10)	-(10)	-(9) 1+(1)	-(9) 1+(1)
Bilirubin	-(8) 1+(1)	-(8) 1+(1)	-(9)	-(10)	-(10)
Blood	-(8) 1+(1)	-(7) 1+(1) 2+(1)	-(8) 1+(2)	-(10)	-(7) 1+(3)
Urobilinogen	<1(8) 1+(1)	<1(8) 1+(1)	<1(8) 1+(2)	<1(10)	<1(8) 1+(2)

[a]Specific gravity is mean±S.D. for 10 rats/group. All other values are expressed as number of rats in parentheses having stated value. For some dose groups and parameters the total does not equal 10 because of insufficient quantity. - Indicates not detectable.

TABLE 18

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Urinalysis[a] - Females at Terminal Sacrifice

	Dose (mg/kg/day)				
	0.0	0.01	0.1	0.5	2.0
Specific Gravity	1.041 ±0.015	1.035[b] ±0.009	1.033 ±0.011	1.039 ±0.010	1.043[b] ±0.011
pH	6.5(3) 7.0(5) 7.5(1) 8.0(1)	7.0(2) 7.5(5) 8.0(1) 8.5(1)	6.5(3) 7.0(1) 7.5(1) 8.0(3) 9.0(1) 9.5(1)	7.0(6) 7.5(3) 8.0(1)	6.0(2) 6.5(1) 7.0(2) 7.5(2) 8.0(1)
Protein	Trace (1) 1+(4) 2+(4) 3+(1)	1+(2) 2+(6) 3+(1)	Trace (1) 1+(4) 2+(4) 3+(1)	Trace (1) 2+(5) 3+(3)	1+(3) 2+(5)
Glucose	-(9) +(1)	-(9)	-(10)	-(8) +(1)	-(8)
Ketones	-(9)	-(9)	-(9) 1+(1)	-(9)	-(8)
Bilirubin	-(10)	-(9)	-(7) 1+(1)	-(8)	-(6) 1+(2)
Blood	-(10)	-(8) 1+(1)	-(8)	-(7) 3+(1)	-(5) 1+(1) 2+(1) 4+(1)
Urobilinogen	<1(7) 1+(2)	<1(8) 1+(1)	<1(6) 1+(2)	<1(9)	<1(4) 1+(3) 3+(1)

[a]Specific gravity is mean±S.D. for 10 rats/group except where noted. All other values are expressed as number of rats in parentheses having stated value. For some dose groups and parameters the total does not equal 10 because of insufficient quantity. - Indicates not detectable.

[b]Value is mean±S.D. for only 9 rats/group due to insufficient quantity of tenth sample.

TABLE 19

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Organ Weight and Organ/Body Weight Ratios[a] - Males at Terminal Sacrifice

Dose (mg/kg/day)	Number of Rats	Fasted Body Weight	Brain		Heart		Kidneys		Liver		Testes	
			g	g/100	g	g/100	g	g/100	g	g/100	g	g/100
0	42	403.2 ±36.1	2.017 ±0.059	0.504 ±0.041	1.050 ±0.069	0.262 ±0.021	3.150 ±0.270	0.786 ±0.086	11.673 ±1.562	2.904 ±0.372	5.004 ±2.028	1.245 ±0.504
0.01	47	417.2 ±39.2	2.035 ±0.067	0.492 ±0.052	1.062 ±0.077	0.256 ±0.022	3.325 ±0.681	0.804 ±0.186	12.140 ±2.257	2.929 ±0.501	4.992 ±1.622	1.205 ±0.407
0.1	45	413.3 ±36.9	2.012 ±0.053	0.490 ±0.043	1.090 ±0.092	0.265 ±0.029	3.215 ±0.390	0.783 ±0.111	11.672 ±1.506	2.840 ±0.416	4.652 ±1.583	1.134 ±0.392
0.5	41	408.7 ±24.9	2.016 ±0.055	0.495 ±0.031	1.099 ±0.113	0.270 ±0.030	3.234 ±0.321	0.793 ±0.086	12.141 ±1.912	2.978 ±0.481	4.655 ±1.715	1.139 ±0.422
2.0	34	384.6 ±22.7	1.979 ±0.058	0.516 ±0.033	1.067 ±0.077	0.278 ±0.023	3.081 ±0.264	0.802 ±0.064	12.468 ±2.040	3.255 ±0.599	4.895 ±1.457	1.279 ±0.391

[a]Data presented as mean±S.D. Statistical analyses not reported.

TABLE 20

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Organ Weight and Organ/Body Weight Ratios[a] - Females at Terminal Sacrifice

Dose (mg/kg/day)	Number of Rats	Fasted Body Weight	Brain		Heart		Kidneys		Liver	
			g	g/100	g	g/100	g	g/100	g	g/100
0	50	272.4 ±27.7	1.830 ±0.064	0.679 ±0.078	0.791 ±0.051	0.293 ±0.028	2.024 ±0.184	0.750 ±0.096	7.274 ±1.569	2.682 ±0.561
0.01	47	274.7 ±25.9	1.820 ±0.053	0.669 ±0.076	0.799 ±0.054	0.294 ±0.041	2.108 ±0.300	0.775 ±0.156	7.543 ±1.130	2.758 ±0.414
0.1	46	283.5 ±25.9	1.837 ±0.050	0.654 ±0.071	0.804 ±0.058	0.287 ±0.043	2.069 ±0.192	0.734 ±0.084	7.367 ±1.090	2.615 ±0.439
0.5	41	281.6 ±23.1	1.818 ±0.058	0.651 ±0.063	0.822 ±0.054	0.294 ±0.026	2.084 ±0.149	0.743 ±0.061	7.674 ±0.995	2.728 ±0.304
2.0	29	266.6 ±28.1	1.806 ±0.050	0.685 ±0.079	0.825 ±0.067	0.312 ±0.034	2.138 ±0.320	0.813 ±0.180	8.392 ±2.511	3.167 ±0.951

[a]Data presented as mean±S.D. Statistical analyses not reported.

TABLE 21

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
EXTERNAL AND SKIN NO LESIONS RECOGNIZED.	0	0	5	21	26
	0.01	3	3	20	26
	0.1	0	5	20	25
	0.5	1	2	16	19
	2.0	2	8	17	27
ABSCESS, TAIL:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
ABSCESS, LIP:	0	1	0	0	1
	0.01	0	0	0	0
	0.1	1	0	1	2
	0.5	0	0	0	0
	2.0	0	0	0	0
ABSCESS, PREPUTIAL GLANDS, UNILATERAL:	0	0	0	1	1
	0.01	0	0	3	3
	0.1	0	0	1	1
	0.5	0	0	2	2
	2.0	0	1	2	3
DISTENDED, ABDOMEN:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
HEMATOCYST (HEMATOMA), HEAD:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
HEMORRHAGE OR BLOOD, VARIOUS LOCATORS:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	1	0	1
NECROSIS, TAIL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
EXTERNAL AND SKIN (CONTINUED)					
ULCER, BACK, FOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
ULCER, LIP:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
CYST(S) WITH KERATINOUS DEBRIS, VARIOUS LOCATORS:	0	1	0	1	2
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	1	1	2
	2.0	0	1	1	2
ABSENT, HIND FOOT, UNILATERAL:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
ALOPECIA, BACK, FOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
CANNABALISM:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
CYST - DARK, VARIOUS LOCATORS:	0	0	0	1	1
	0.01	0	0	3	3
	0.1	0	0	4	4
	0.5	0	0	4	4
	2.0	0	0	1	1
CYST - DARK, VARIOUS LOCATORS, MULTIFOCAL:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
EXTERNAL AND SKIN (CONTINUED)					
CALCULUS(I) SAND-LIKE, PREPUTIAL:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
FACIAL SOILING - CLEAR:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
FACIAL SOILING - PORPHYRIN, VARIOUS LOCATORS:	0	1	1	1	3
	0.01	3	0	1	4
	0.1	0	1	0	1
	0.5	1	2	0	3
	2.0	0	2	0	2
ICTERUS:	0	0	3	0	3
	0.01	0	3	0	3
	0.1	0	2	0	2
	0.5	0	5	1	6
	2.0	1	3	0	4
PERINEAL SOILING:	0	1	2	0	3
	0.01	0	0	0	0
	0.1	0	2	0	2
	0.5	1	3	0	4
	2.0	0	1	0	1
ROUGH HAIRCOAT:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
SOILED HAIRCOAT, VARIOUS LOCATORS:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
TRAUMA, TAIL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
EXTERNAL AND SKIN (CONTINUED)					
TRAUMA, HIND FOOT, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
VERRUCOUS THICKENING, VARIOUS LOCATORS (EXCLUDING HIND FOOT PAD):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	1	1
	2.0	0	0	1	1
VERRUCOUS THICKENING, HIND FOOT PAD, UNILATERAL:	0	0	0	11	11
	0.01	0	0	9	9
	0.1	0	0	10	10
	0.5	0	0	11	11
	2.0	0	0	7	7
VERRUCOUS THICKENING, HIND FOOT PAD, BILATERAL:	0	0	0	1	1
	0.01	0	0	1	1
	0.1	0	0	2	2
	0.5	0	0	1	1
	2.0	0	0	0	0
ULCER, HIND FOOT PAD, UNILATERAL:	0	0	2	2	4
	0.01	0	0	9	9
	0.1	1	0	5	6
	0.5	0	0	5	5
	2.0	0	0	6	6
ULCER, HIND FOOT PAD, BILATERAL:	0	0	0	4	4
	0.01	0	0	1	1
	0.1	0	0	1	1
	0.5	0	0	2	2
	2.0	0	0	0	0
ABSCESS, HIND FOOT PAD, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	1	1
SCAB OR SCALES, VARIOUS LOCATORS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	1	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
EXTERNAL AND SKIN (CONTINUED)					
PALE AND/OR PALE - ANEMIC:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	1	1
	2.0	1	0	0	1
MASS / NODULE:	0	0	2	2	4
	0.01	0	1	2	3
	0.1	0	3	3	6
	0.5	0	1	7	8
	2.0	0	4	2	6
MASS / NODULE, (TWO):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	1	0	1
	2.0	0	0	0	0
LIVER NO LESIONS RECOGNIZED.	0	1	2	36	39
	0.01	3	1	36	40
	0.1	1	1	36	38
	0.5	1	4	34	39
	2.0	1	3	21	25
ACCENTUATED LOBULAR PATTERN:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
CONGESTION, VARIOUS DESCRIPTORS:	0	0	1	0	1
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
DECREASED SIZE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	2	0	2
	2.0	0	0	0	0
INCREASED SIZE, VARIOUS GRADES:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	3	0	3
	2.0	0	2	2	4

[a] Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
LIVER (CONTINUED)					
TOTAL NUMBER OF ANIMALS WITH AN AREA OF ANY TYPE, ANY LOCATION, FOCAL OR MULTIFOCAL:	0	0	2	0	2
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	1	0	0	1
FIRM, ONE LOBE, FOCAL - SLIGHT:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
FOCUS - DARK, VARIOUS LOCATORS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	2	3
	0.5	0	0	0	0
	2.0	0	2	1	3
FOCUS - DARK, VARIOUS LOCATORS, MULTIFOCAL:	0	0	2	0	2
	0.01	0	0	2	2
	0.1	0	1	1	2
	0.5	0	1	0	1
	2.0	0	0	0	0
FOCUS - DARK DEPRESSED, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - DARK ELEVATED, ONE LOBE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - ELEVATED, VARIOUS LOCATORS:	0	0	1	1	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - ELEVATED, VARIOUS LOCATORS, MULTIFOCAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
LIVER (CONTINUED)					
FOCUS - PALE, VARIOUS LOCATORS:	0	0	0	3	3
	0.01	0	0	1	1
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	1	4	5
FOCUS - PALE, VARIOUS LOCATORS, MULTIFOCAL:	0	0	1	0	1
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	2	1	3
	2.0	0	0	0	0
FOCUS - PALE ELEVATED, VARIOUS LOCATORS:	0	0	1	1	2
	0.01	0	0	1	1
	0.1	0	0	1	1
	0.5	0	0	1	1
	2.0	0	0	0	0
TOTAL NUMBER OF ANIMALS WITH A FOCUS(I) OF ANY TYPE, ANY LOCATION:	0	0	6	4	10
	0.01	1	0	4	5
	0.1	0	3	6	9
	0.5	0	3	2	5
	2.0	0	3	5	8
HERNIA, LEFT MIDDLE LOBE, CRANIAL SURFACE:	0	0	1	1	2
	0.01	0	0	2	2
	0.1	0	2	2	4
	0.5	0	0	0	0
	2.0	0	0	0	0
INCREASED SIZE - PROBABLY LYMPHORETICULAR TUMOR:	0	0	2	0	2
	0.01	2	4	2	8
	0.1	1	3	0	4
	0.5	0	1	1	2
	2.0	0	2	1	3
MOTTLED, VARIOUS DESCRIPTORS:	0	0	2	0	2
	0.01	1	2	0	3
	0.1	0	3	0	3
	0.5	1	5	0	6
	2.0	1	4	0	5
PALE, VARIOUS DESCRIPTORS:	0	0	5	0	5
	0.01	1	0	1	2
	0.1	0	3	1	4
	0.5	1	2	1	4
	2.0	1	9	1	11

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
LIVER (CONTINUED)					
ROUGHENED SURFACE:	0	0	3	4	7
	0.01	1	2	5	8
	0.1	0	1	2	3
	0.5	0	0	7	7
	2.0	0	6	9	15
MASS / NODULE:	0	0	1	0	1
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	2	3	5
HEART NO LESIONS RECOGNIZED.	0	1	11	39	51
	0.01	7	5	35	47
	0.1	2	11	41	54
	0.5	2	13	39	54
	2.0	3	18	33	54
DILATED - MODERATE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
THROMBUS - ANY TYPE, ATRIUM, LEFT:	0	0	2	0	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
FOCUS - PALE, VENTRICLE:	0	0	1	1	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
FOCUS - PALE, VENTRICLE, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
PALE AND/OR FOCUS - PALE, PAPILLARY MUSCLE:	0	0	1	4	5
	0.01	0	1	11	12
	0.1	0	0	3	3
	0.5	0	0	5	5
	2.0	0	2	2	4

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
HEART (CONTINUED)					
FOCUS - PALE ELEVATED, VENTRICLE:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	2	2
	0.5	0	0	0	0
	2.0	0	0	0	0
MOTTLED, ATRIUM, LEFT:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
SPLEEN NO LESIONS RECOGNIZED.	0	1	9	39	49
	0.01	4	1	34	39
	0.1	1	7	37	45
	0.5	2	6	33	41
	2.0	2	9	24	35
ADHESIONS, CAPSULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
FIBROSIS, CAPSULE, FOCAL:	0	0	1	0	1
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
INCREASED SIZE - UNSPECIFIED DEGREE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
INCREASED SIZE - SLIGHT:	0	0	1	1	2
	0.01	1	0	8	9
	0.1	0	0	3	3
	0.5	0	1	5	6
	2.0	0	3	3	6
INCREASED SIZE - MODERATE:	0	0	1	2	3
	0.01	0	0	3	3
	0.1	0	1	3	4
	0.5	0	0	3	3
	2.0	0	0	4	4

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
SPLEEN (CONTINUED)					
INCREASED SIZE - SEVERE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
AREA - PALE DEPRESSED:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	2	2
FIRM:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
FOCUS - PALE DEPRESSED:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	2	2
	2.0	0	0	0	0
FOCUS - PALE ELEVATED:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
INCREASED SIZE - PROBABLY LYMPHORETICULAR TUMOR, VARIOUS GRADES:	0	0	4	0	4
	0.01	2	5	2	9
	0.1	1	4	2	7
	0.5	0	6	2	8
	2.0	1	6	3	10
MOTTLED:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
ROUGHENED SURFACE:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
SPLEEN (CONTINUED)					
RUPTURED, CAPSULE:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	1	0	1
BRAIN NO LESIONS RECOGNIZED.	0	1	14	43	58
	0.01	4	5	46	55
	0.1	1	9	44	54
	0.5	1	13	40	54
	2.0	4	18	35	57
HEMORRHAGE, VARIOUS LOCATORS, FOCAL OR MULTIFOCAL:	0	0	0	0	0
	0.01	1	1	0	2
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
COLOR - GRAY AND MALACIC, CEREBRUM, LEFT, FOCAL - MODERATE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
COMPRESSION SECONDARY TO PITUITARY MASS:	0	0	0	1	1
	0.01	0	0	1	1
	0.1	0	1	2	3
	0.5	1	0	4	5
	2.0	0	0	0	0
FOCUS - DARK, VARIOUS LOCATORS:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	1	1	0	2
	0.5	0	1	0	1
	2.0	0	0	0	0
FOCUS - DARK, VARIOUS LOCATORS, MULTIFOCAL:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	1	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
BRAIN (CONTINUED)					
MASS / NODULE:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
PITUITARY NO LESIONS RECOGNIZED.	0	1	13	29	43
	0.01	7	4	33	44
	0.1	2	10	28	40
	0.5	1	12	35	48
	2.0	4	12	26	42
INCREASED SIZE - SLIGHT:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
CYST - CLEAR:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - DARK:	0	0	1	7	8
	0.01	0	1	7	8
	0.1	0	1	6	7
	0.5	0	1	3	4
	2.0	0	5	4	9
FOCUS - DARK, MULTIFOCAL:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - PALE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
MASS / NODULE:	0	0	1	8	9
	0.01	0	0	6	6
	0.1	0	1	12	13
	0.5	1	1	6	8
	2.0	0	2	5	7

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
SPINAL CORD NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
PERIPHERAL NERVE NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
PANCREAS NO LESIONS RECOGNIZED.	0	1	14	41	56
	0.01	7	5	47	59
	0.1	2	9	44	55
	0.5	2	13	40	55
	2.0	4	20	33	57
FOCUS - PALE, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	2	2
	0.01	0	1	0	1
	0.1	0	3	2	5
	0.5	0	0	4	4
	2.0	0	1	2	3
MASS / NODULE, (TWO):	0	0	1	1	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
BONE NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	1	11	46	58
	0.5	2	14	44	60
	2.0	4	21	35	60
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	1	0	2
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
ADRENAL					
NO LESIONS RECOGNIZED.	0	1	15	42	58
	0.01	7	6	47	60
	0.1	1	11	41	53
	0.5	2	14	42	58
	2.0	4	20	34	58
HEMATOCYST (HEMATOMA), UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0
INCREASED SIZE, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
FOCUS - DARK, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	2	2
	0.01	0	0	0	0
	0.1	1	0	4	5
	0.5	0	0	1	1
	2.0	0	1	1	2
KIDNEY					
NO LESIONS RECOGNIZED.	0	1	8	12	21
	0.01	6	3	15	24
	0.1	1	6	17	24
	0.5	2	6	16	24
	2.0	2	9	10	21
CONGESTION, VARIOUS DESCRIPTORS:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
DILATED, PELVIS, BILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
KIDNEY (CONTINUED)					
INCREASED SIZE, BILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
AREA - PALE, BILATERAL, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
DARK:	0	0	2	0	2
	0.01	0	3	0	3
	0.1	0	2	0	2
	0.5	0	4	0	4
	2.0	1	2	1	4
FOCUS - DARK DEPRESSED, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
FOCUS - PALE, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	1	0	1
	2.0	0	0	0	0
PALE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	2	0	2
	2.0	0	0	0	0
ROUGHENED SURFACE - UNSPECIFIED DEGREE:	0	0	2	0	2
	0.01	0	0	0	0
	0.1	0	3	0	3
	0.5	0	2	0	2
	2.0	0	5	0	5
ROUGHENED SURFACE - SLIGHT:	0	0	1	30	31
	0.01	1	0	25	26
	0.1	0	0	25	25
	0.5	0	0	26	25
	2.0	0	4	22	26

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
KIDNEY (CONTINUED)					
ROUGHENED SURFACE - MODERATE:	0	0	1	2	3
	0.01	0	0	6	6
	0.1	0	0	4	4
	0.5	0	0	2	2
	2.0	0	0	1	1
ROUGHENED SURFACE - SEVERE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	1	2
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	2	2
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
ORAL CAVITY NO LESIONS RECOGNIZED.	0	1	15	42	58
	0.01	7	5	44	56
	0.1	2	10	45	57
	0.5	2	14	41	57
	2.0	4	20	31	55
EXUDATE - MUCOID, HARD PALATE - SLIGHT:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
INFLAMMATION - CASEOUS, SOFT PALATE, FOCAL - MODERATE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
MALOCCLUSION:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
OVERGROWN INCISORS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	2	1	3
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
ORAL CAVITY (CONTINUED)					
VERRUCOUS THICKENING, HARD PALATE:	0	0	0	1	1
	0.01	0	0	2	2
	0.1	0	0	0	0
	0.5	0	0	2	2
	2.0	0	0	3	3
MASS / NODULE:	0	0	0	1	1
	0.01	0	1	1	2
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	1	1
TONGUE NO LESIONS RECOGNIZED.	0	1	15	42	58
	0.01	7	6	43	56
	0.1	2	12	46	60
	0.5	2	14	43	59
	2.0	4	21	35	60
VERRUCOUS THICKENING:	0	0	0	0	0
	0.01	0	0	2	2
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	2	2
	0.01	0	0	2	2
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
ESOPHAGUS NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
STOMACH NO LESIONS RECOGNIZED.	0	1	7	43	51
	0.01	3	5	45	53
	0.1	1	2	44	47
	0.5	0	4	41	45
	2.0	4	9	34	47

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
STOMACH (CONTINUED)					
EDEMA, WALL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
HEMORRHAGE, GLANDULAR MUCOSA - VERY SLIGHT:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
THICKENED WALL, VARIOUS DESCRIPTORS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	3	0	3
	0.5	0	0	0	0
	2.0	0	3	0	3
ULCER AND/OR EROSION, GLANDULAR MUCOSA:	0	0	1	1	2
	0.01	0	0	1	1
	0.1	0	1	0	1
	0.5	0	1	1	2
	2.0	0	1	0	1
ULCER AND/OR EROSION, GLANDULAR MUCOSA, MULTIFOCAL:	0	0	4	0	4
	0.01	3	0	0	3
	0.1	1	2	2	5
	0.5	0	2	0	2
	2.0	0	6	0	6
ULCER AND/OR EROSION, NONGLANDULAR MUCOSA:	0	0	1	0	1
	0.01	1	0	1	2
	0.1	0	3	0	3
	0.5	1	1	1	3
	2.0	0	0	0	0
ULCER AND/OR EROSION, NONGLANDULAR MUCOSA, MULTIFOCAL:	0	0	0	0	0
	0.01	2	0	0	2
	0.1	0	3	0	3
	0.5	0	2	0	2
	2.0	0	4	0	4
ULCER - PERFORATED, NONGLANDULAR MUCOSA:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	1	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
STOMACH (CONTINUED)					
DECREASED INGESTA:	0	0	1	0	1
	0.01	1	1	0	2
	0.1	0	1	0	1
	0.5	1	2	0	3
	2.0	0	0	0	0
FOCUS - DARK, VARIOUS LOCATORS, FOCAL OR MULTIFOCAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	1	0	1
GAS:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
HEMOLYZED BLOOD, VARIOUS DESCRIPTORS:	0	0	2	0	2
	0.01	1	0	0	1
	0.1	0	2	0	2
	0.5	1	3	0	4
	2.0	0	1	0	1
VERRUCOUS THICKENING, NONGLANDULAR MUCOSA:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
SMALL INTESTINE NO LESIONS RECOGNIZED.	0	1	13	44	58
	0.01	7	5	47	59
	0.1	1	9	46	56
	0.5	1	11	44	56
	2.0	4	20	33	57
DILATED, FOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
SMALL INTESTINE (CONTINUED)					
EDEMA, ILEUM WALL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
DECREASED INGESTA:	0	0	1	0	1
	0.01	0	1	0	1
	0.1	0	3	0	3
	0.5	1	2	0	3
	2.0	0	0	0	0
FOCUS - PALE ELEVATED, JEJUNUM, FOCAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
GAS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	1	0	1
HEMOLYZED BLOOD:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	1	0	1
	2.0	0	0	1	1
CECUM NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	5	47	59
	0.1	2	11	46	59
	0.5	2	13	44	59
	2.0	3	20	35	58
DISTENDED - MODERATE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
EDEMA, WALL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
CECUM (CONTINUED)					
DECREASED INGESTA:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	1	0	1
	0.5	0	1	0	1
	2.0	0	0	0	0
GAS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	1	0	1
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
COLON NO LESIONS RECOGNIZED.	0	1	15	43	59
	0.01	7	6	47	60
	0.1	2	11	45	58
	0.5	2	13	44	59
	2.0	4	19	34	57
DECREASED INGESTA:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
GAS - SEVERE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
MASS / NODULE:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	1	1	2
	0.5	0	0	0	0
	2.0	0	1	1	2
RECTUM NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60

[a] Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
TESTICLE					
NO LESIONS RECOGNIZED.	0	1	0	0	1
	0.01	5	0	1	6
	0.1	0	0	2	2
	0.5	1	0	2	3
	2.0	2	1	0	3
ATROPHY OR DECREASED SIZE, UNILATERAL, VARIOUS GRADES:	0	0	4	6	10
	0.01	0	2	4	6
	0.1	1	2	4	7
	0.5	0	1	2	3
	2.0	0	3	5	8
ATROPHY OR DECREASED SIZE, BILATERAL, VARIOUS GRADES:	0	0	4	0	4
	0.01	0	0	0	0
	0.1	1	2	1	4
	0.5	1	5	0	6
	2.0	1	4	0	5
INCREASED SIZE, BILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
AREA - PALE, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
FLACCID:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	2	0	2
	0.5	0	0	0	0
	2.0	1	1	0	2
FOCUS - PALE, FOCAL OR MULTIFOCAL:	0	0	1	1	2
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
MASS / NODULE:	0	0	13	43	56
	0.01	2	6	46	54
	0.1	1	11	43	55
	0.5	0	14	42	56
	2.0	1	19	35	55

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
EPIDIDYMIS					
NO LESIONS RECOGNIZED.	0	1	14	44	59
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	13	44	59
	2.0	4	21	35	60
ABSCESS, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
INCREASED SIZE, HEAD, UNILATERAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
SEMINAL VESICLE					
NO LESIONS RECOGNIZED.	0	0	10	44	54
	0.01	7	4	47	58
	0.1	2	7	46	55
	0.5	2	10	44	56
	2.0	3	16	35	54
ATROPHY OR DECREASED SIZE, VARIOUS GRADES:	0	0	5	0	5
	0.01	0	2	0	2
	0.1	0	5	0	5
	0.5	0	4	0	4
	2.0	1	5	0	6
DISTENDED - MODERATE:	0	1	0	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
INFLAMMATION - PURULENT, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
COAGULATING GLAND					
NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	13	44	59
	2.0	4	21	35	60

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
COAGULATING GLAND (CONTINUED)					
ATROPHY, BILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
PROSTATE NO LESIONS RECOGNIZED.	0	0	13	36	49
	0.01	7	6	43	56
	0.1	2	12	38	52
	0.5	2	11	42	55
	2.0	4	20	29	53
ABSCESS:	0	0	2	0	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
ATROPHY:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
INFLAMMATION - VARIOUS DESCRIPTORS:	0	1	0	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	1	0	1
MOTTLED:	0	0	0	8	8
	0.01	0	0	4	4
	0.1	0	0	8	8
	0.5	0	0	2	2
	2.0	0	0	6	6
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
URINARY BLADDER NO LESIONS RECOGNIZED.	0	0	15	44	59
	0.01	6	5	47	58
	0.1	2	12	46	60
	0.5	2	13	44	59
	2.0	4	20	34	58

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
URINARY BLADDER (CONTINUED)					
DISTENDED:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
HEMORRHAGE, MUCOSA, MULTIFOCAL:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
THICKENED, WALL:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
EXUDATE - CLOUDY, LUMEN:	0	1	0	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
ROUGHENED SURFACE, MUCOSA - MODERATE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
URINE - DARK:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	1	0	1
URETER NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
URETHRA NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
LUNGS					
NO LESIONS RECOGNIZED.	0	0	8	41	49
	0.01	3	5	42	50
	0.1	0	8	44	52
	0.5	1	10	41	52
	2.0	2	18	35	55
ATELECTASIS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	1	0	0	1
CONGESTION OR DARK, VARIOUS DESCRIPTORS:	0	1	2	0	3
	0.01	2	0	0	2
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
EDEMA:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	1	0	0	1
	2.0	1	0	0	1
HEMORRHAGE, ONE LOBE, MULTIFOCAL - MODERATE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
MINERALIZATION, ONE LOBE, FOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
AREA - DARK, ONE LOBE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
CONSOLIDATION, ONE LOBE, DIFFUSE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
LUNGS (CONTINUED)					
FAILURE TO COLLAPSE:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - DARK, MULTIFOCAL:	0	0	2	1	3
	0.01	2	1	2	5
	0.1	1	1	0	2
	0.5	0	2	0	2
	2.0	0	1	0	1
FOCUS - DEPRESSED, ONE LOBE:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS-GRAY, ONE LOBE, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - PALE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
FOCUS - PALE, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
FOCUS - PALE ELEVATED, ONE LOBE:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
MOTTLED, GENERALIZED - MODERATE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
LUNGS (CONTINUED)					
PETECHIA, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
ASPIRATED BLOOD - SECONDARY TO DECAPITATION:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	1	0	0	1
	2.0	0	0	0	0
MASS / NODULE:	0	0	2	2	4
	0.01	0	0	0	0
	0.1	1	1	2	4
	0.5	0	1	0	1
	2.0	0	1	0	1
MASS / NODULE, (TWO):	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
LARYNX NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
TRACHEA NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
SKELETAL MUSCLE NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	6	6	47	59
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
SKELETAL MUSCLE (CONTINUED)					
HEMORRHAGE, VARIOUS LOCATORS, MULTIFOCAL:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
SALIVARY GLAND NO LESIONS RECOGNIZED.	0	1	15	43	59
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
MASS / NODULE:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
THYMUS NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	13	44	59
	2.0	4	20	35	59
DECREASED SIZE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
INCREASED SIZE - PROBABLY LYMPHORETICULAR TUMOR:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
AORTA NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	20	35	59

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
AORTA (CONTINUED)					
MINERALIZATION:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
THYROID GLAND NO LESIONS RECOGNIZED.	0	1	13	43	57
	0.01	7	6	47	60
	0.1	2	11	41	54
	0.5	2	14	41	57
	2.0	4	18	31	53
INCREASED SIZE, UNILATERAL:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	1	1
	2.0	0	0	0	0
MASS / NODULE:	0	0	2	0	2
	0.01	0	0	0	0
	0.1	0	1	4	5
	0.5	0	0	2	2
	2.0	0	3	4	7
PARATHYROID GLAND NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
MAMMARY GLAND NO LESIONS RECOGNIZED.	0	1	14	37	52
	0.01	7	5	41	53
	0.1	2	10	37	49
	0.5	2	14	39	55
	2.0	4	19	28	51
GALACTOCELE:	0	0	0	2	2
	0.01	0	0	1	1
	0.1	0	0	2	2
	0.5	0	0	1	1
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
MAMMARY GLAND (CONTINUED)					
GALACTOCELE, (TWO):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	1	1
MASS / NODULE:	0	0	1	5	6
	0.01	0	1	5	6
	0.1	0	0	7	7
	0.5	0	0	4	4
	2.0	0	1	6	7
MASS / NODULE, (THREE):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	1	0	1
EYE NO LESIONS RECOGNIZED.	0	1	13	40	54
	0.01	5	6	45	56
	0.1	2	11	43	56
	0.5	2	13	40	55
	2.0	4	19	33	56
INCREASED SIZE, UNILATERAL:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
NECROSIS, CORNEA, UNILATERAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
ULCER, CORNEA, UNILATERAL:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
CLOUDY, CORNEA, UNILATERAL:	0	0	0	2	2
	0.01	1	0	1	2
	0.1	0	1	0	1
	0.5	0	0	2	2
	2.0	0	1	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
EYE (CONTINUED)					
CLOUDY, CORNEA, BILATERAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
EXOPHTHALMIA, UNILATERAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
EXUDATE-RED, EYELID, UNILATERAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
OPACITY, LENS, UNILATERAL, DIFFUSE - SEVERE:	0	0	0	1	1
	0.01	0	0	1	1
	0.1	0	0	3	3
	0.5	0	0	0	0
	2.0	0	1	1	2
OPACITY, LENS, BILATERAL, DIFFUSE - SEVERE	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
VERRUCOUS THICKENING, EYELID, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
MASS / NODULE (EYELID):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
MASS / NODULE (POSSIBLY LACRIMAL GLAND):	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
NASAL TURBINATES NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	11	46	59
	0.5	2	14	44	60
	2.0	4	21	35	60
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
LACRIMAL GLAND NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
ZYMBAL GLAND NO LESIONS RECOGNIZED.	0	1	15	44	60
	0.01	7	6	46	59
	0.1	2	10	45	57
	0.5	2	14	44	60
	2.0	4	19	35	58
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	2	1	3
	0.5	0	0	0	0
	2.0	0	2	0	2
ABDOMINAL CAVITY NO LESIONS RECOGNIZED.	0	1	6	35	42
	0.01	6	4	40	50
	0.1	1	4	34	39
	0.5	2	7	38	47
	2.0	2	14	28	44
ADHESIONS - FIBROUS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
HEMORRHAGE OR HEMOPERITONEUM:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
ABDOMINAL CAVITY (CONTINUED)					
ASCITES - CLEAR:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
ASCITES - SEROSANGUINEOUS:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	2	2
	0.5	0	2	0	2
	2.0	0	1	1	2
CYST - CLEAR:	0	0	1	0	1
	0.01	0	0	1	1
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0
EXUDATE - CLOUDY - SLIGHT:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
FAT - DECREASED AMOUNT, VARIOUS GRADES:	0	0	5	1	6
	0.01	0	0	3	3
	0.1	1	6	3	10
	0.5	0	3	0	3
	2.0	0	4	2	6
FAT - STRANGULATED OR NECROTIC PORTION:	0	0	2	6	8
	0.01	1	0	2	3
	0.1	1	1	3	5
	0.5	0	1	1	2
	2.0	0	0	2	2
FAT - STRANGULATED OR NECROTIC PORTION, (TWO):	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - DARK, MESENTERY, MULTIFOCAL:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
ABDOMINAL CAVITY (CONTINUED)					
ACCESSORY SPLEEN:	0	0	0	2	2
	0.01	0	0	0	0
	0.1	0	0	2	2
	0.5	0	0	4	4
	2.0	1	0	0	1
MASS / NODULE:	0	0	1	1	2
	0.01	0	0	0	0
	0.1	0	1	4	5
	0.5	0	3	1	4
	2.0	0	2	3	5
LYMPH NODES NO LESIONS RECOGNIZED.	0	1	14	43	58
	0.01	6	5	47	58
	0.1	2	12	45	59
	0.5	2	11	44	57
	2.0	3	16	34	53
ABSCESS, MESENTERIC: - SLIGHT	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
INCREASED SIZE, INDIVIDUAL LYMPH NODE:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	3	1	4
FIRM, MEDIASTINAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
INCREASED SIZE - PROBABLY LYMPHORETICULAR TUMOR, ONE OR MORE INDIVIDUAL LYMPH NODES:	0	0	0	0	0
	0.01	1	1	0	2
	0.1	0	0	1	1
	0.5	0	1	0	1
	2.0	0	3	0	3
INCREASED SIZE - PROBABLY METASTATIC TUMOR, ONE OR MORE INDIVIDUAL LYMPH NODES:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	1	0	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
LYMPH NODES (CONTINUED)					
PALE, INDIVIDUAL LYMPH NODE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
MASS / NODULE:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
THORACIC CAVITY NO LESIONS RECOGNIZED.	0	1	11	42	54
	0.01	7	6	47	60
	0.1	2	11	45	58
	0.5	2	11	44	57
	2.0	2	21	35	58
CYST - CLEAR, MEDIASTINAL TISSUE:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
HYDROTHORAX - CLEAR:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
HYDROTHORAX - CLOUDY:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
HYDROTHORAX - SEROSANGUINEOUS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	1	0	0	1
HEMORRHAGE - TERMINAL:	0	0	0	2	2
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 21 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	15	44	60
	0.01	7	6	47	60
	0.1	2	12	46	60
	0.5	2	14	44	60
	2.0	4	21	35	60
THORACIC CAVITY (CONTINUED)					
HEMOTHORAX:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
MASS / NODULE:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	1	0	1
	2.0	0	0	0	0
VASCULATURE NO LESIONS RECOGNIZED.	0	1	15	41	57
	0.01	7	6	46	59
	0.1	2	12	45	59
	0.5	2	14	43	59
	2.0	4	21	34	59
PROMINANT BLOOD VESSELS, PANCREATIC BLOOD VESSELS:	0	0	0	3	3
	0.01	0	0	1	1
	0.1	0	0	1	1
	0.5	0	0	1	1
	2.0	0	0	1	1

[a]Data presented as the number of animals with the stated observation.

TABLE 22

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
EXTERNAL AND SKIN					
NO LESIONS RECOGNIZED.	0	0	2	26	28
	0.01	0	5	27	32
	0.1	2	2	25	29
	0.5	0	7	29	36
	2.0	1	11	16	28
ABSCESS, CLITORAL GLAND, UNILATERAL:	0	0	0	1	1
	0.01	0	0	4	4
	0.1	0	0	1	1
	0.5	0	0	3	3
	2.0	0	0	2	2
ABSCESS, CLITORAL GLAND, BILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
ABSCESS, LIP:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
DISTENDED, ABDOMEN:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
HEMORRHAGE, VARIOUS LOCATIONS:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	1	1	0	2
	0.5	0	0	0	0
	2.0	1	1	0	2
ULCER, FOREFOOT, UNILATERAL:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
ULCER, INGUINAL, FOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
EXTERNAL AND SKIN (CONTINUED)					
CYST(S) WITH KERATINOUS DEBRIS, VARIOUS LOCATIONS:	0	0	1	1	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
EXUDATE - MUCOID, PERINEAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
EXUDATE-RED, VULVA OR PERINEUM:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	1	0	0	1
	2.0	1	0	0	1
FACIAL SOILING - PORPHYRIN VARIOUS LOCATIONS:	0	0	2	3	5
	0.01	0	3	3	6
	0.1	0	0	2	2
	0.5	1	1	0	2
	2.0	0	7	0	7
ICTERUS:	0	0	1	0	1
	0.01	0	1	0	1
	0.1	1	1	0	2
	0.5	0	3	0	3
	2.0	0	4	0	4
PERINEAL SOILING:	0	0	1	1	2
	0.01	0	1	1	2
	0.1	1	0	0	1
	0.5	2	2	1	5
	2.0	0	4	0	4
ROUGH HAIRCOAT:	0	1	0	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
TRAUMA, TAIL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
EXTERNAL AND SKIN (CONTINUED)					
VERRUCOUS THICKENING, VARIOUS LOCATIONS (EXCLUDING HIND FOOT PAD):	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0
VERRUCOUS THICKENING, HIND FOOT PAD, UNILATERAL:	0	0	0	14	14
	0.01	0	0	12	12
	0.1	0	0	13	13
	0.5	0	0	7	7
	2.0	0	0	5	5
VERRUCOUS THICKENING, HIND FOOT PAD, BILATERAL:	0	0	0	1	1
	0.01	0	0	1	1
	0.1	0	0	3	3
	0.5	0	0	3	3
	2.0	0	0	3	3
ULCER, HIND FOOT PAD, UNILATERAL:	0	0	0	2	2
	0.01	0	1	3	4
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	3	3
ULCER, HIND FOOT PAD, BILATERAL:	0	0	0	2	2
	0.01	0	0	1	1
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0
ABSCESS, HIND FOOT PAD, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
SCAB, VARIOUS LOCATIONS:	0	0	1	1	2
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
CRUSTS, TAIL, MULTIFOCAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
EXTERNAL AND SKIN (CONTINUED)					
PALE - ANEMIC:	0	1	0	0	1
	0.01	0	0	1	1
	0.1	1	1	0	2
	0.5	1	1	0	2
	2.0	0	3	0	3
MASS / NODULE:	0	1	2	0	3
	0.01	1	0	0	1
	0.1	1	1	1	3
	0.5	0	2	0	2
	2.0	2	5	0	7
LIVER NO LESIONS RECOGNIZED.	0	1	1	39	41
	0.01	0	4	35	39
	0.1	3	0	37	40
	0.5	3	6	28	37
	2.0	1	15	16	32
ACCENTUATED LOBULAR PATTERN, VARIOUS DESCRIPTORS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	1	0	1
CONGESTION, VARIOUS DESCRIPTORS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
DECREASED SIZE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	2	0	2
	2.0	0	0	0	0
INCREASED SIZE:	0	0	1	0	1
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	2	2
TOTAL NUMBER OF ANIMALS WITH AN AREA OF ANY TYPE, ANY LOCATION	0	0	2	0	2
	0.01	0	2	0	2
	0.1	1	0	0	1
	0.5	0	0	1	1
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
LIVER (CONTINUED)					
FOCUS - DARK, VARIOUS LOCATORS:	0	0	0	2	2
	0.01	0	0	1	1
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	1	0	1
FOCUS - DARK, VARIOUS LOCATORS, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
FOCUS - DARK DEPRESSED, VARIOUS LOCATORS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - ELEVATED, VARIOUS LOCATORS:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
FOCUS - PALE, VARIOUS LOCATORS:	0	0	1	3	4
	0.01	0	1	1	2
	0.1	0	0	1	1
	0.5	0	1	1	2
	2.0	0	1	1	2
FOCUS - PALE, VARIOUS LOCATORS, MULTIFOCAL:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	1	1	2
	2.0	0	4	0	4
FOCUS - PALE ELEVATED, VARIOUS LOCATORS:	0	0	0	1	1
	0.01	0	0	1	1
	0.1	0	0	2	2
	0.5	0	0	2	2
	2.0	0	0	3	3
FOCUS - PALE ELEVATED, VARIOUS LOCATORS, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	1	2

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	8	50	60
NECROPSIED DURING	0.01	2	10	48	60
THE TIME PERIOD	0.1	8	5	47	60
INDICATED	0.5	4	13	43	60
	2.0	4	28	29	61
LIVER (CONTINUED)					
TOTAL NUMBER OF ANIMALS WITH A FOCUS(I) OF ANY TYPE, ANY LOCATION:	0	0	2	7	9
	0.01	0	1	3	4
	0.1	0	2	4	6
	0.5	0	2	4	6
	2.0	0	8	6	14
HERNIA, LEFT MIDDLE LOBE, CRANIAL SURFACE:	0	0	1	3	4
	0.01	0	1	2	3
	0.1	2	1	4	7
	0.5	0	1	7	8
	2.0	0	3	2	5
INCREASED SIZE - PROBABLY LYMPHORETICULAR TUMOR:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	2	0	3
	0.5	0	1	0	1
	2.0	0	0	0	0
MOTTLED:	0	1	2	0	3
	0.01	0	2	0	2
	0.1	0	1	0	1
	0.5	0	1	0	1
	2.0	0	5	4	9
PALE, VARIOUS GRADES:	0	0	4	0	4
	0.01	1	2	2	5
	0.1	3	2	0	5
	0.5	1	2	0	3
	2.0	3	3	3	9
PALE, INDIVIDUAL LOBE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
ROUGHENED SURFACE:	0	1	1	4	6
	0.01	0	2	7	9
	0.1	1	0	2	3
	0.5	0	3	5	8
	2.0	0	1	1	2
MASS / NODULE:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
HEART					
NO LESIONS RECOGNIZED.	0	2	7	48	57
	0.01	2	10	46	58
	0.1	8	4	46	58
	0.5	4	13	43	60
	2.0	4	25	28	57
INCREASED SIZE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
THICKENED, ATRIUM, LEFT:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
FOCUS - PALE, VENTRICLE:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	2	0	2
PALE AND/OR FOCUS - PALE, PAPILLARY MUSCLE, LEFT:	0	0	0	2	2
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - PALE ELEVATED, VENTRICLE:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
PALE, ATRIUM, LEFT:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
SPLEEN					
NO LESIONS RECOGNIZED.	0	0	5	44	49
	0.01	1	5	40	46
	0.1	4	2	44	50
	0.5	2	10	37	49
	2.0	3	17	23	43

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
SPLEEN (CONTINUED)					
INCREASED SIZE - UNSPECIFIED DEGREE:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	2	0	2
INCREASED SIZE - SLIGHT:	0	1	0	2	3
	0.01	0	2	5	7
	0.1	3	0	1	4
	0.5	1	0	2	3
	2.0	1	3	4	8
INCREASED SIZE - MODERATE:	0	0	0	2	2
	0.01	0	1	2	3
	0.1	0	0	1	1
	0.5	1	0	3	4
	2.0	0	1	2	3
PALE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - PALE DEPRESSED:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
INCREASED SIZE - PROBABLY LYMPHORETICULAR TUMOR - VARIOUS GRADES:	0	1	2	1	4
	0.01	1	2	1	4
	0.1	1	2	1	4
	0.5	0	3	1	4
	2.0	0	5	0	5
ROUGHENED SURFACE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
RUPTURED, CAPSULE:	0	0	1	0	1
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
BRAIN					
NO LESIONS RECOGNIZED.	0	2	4	46	52
	0.01	2	8	43	53
	0.1	5	4	41	50
	0.5	4	8	36	48
	2.0	4	19	27	50
HEMORRHAGE, VARIOUS LOCATORS, FOCAL OR MULTIFOCAL:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
COMPRESSION SECONDARY TO PITUITARY MASS:	0	0	3	4	7
	0.01	0	1	5	6
	0.1	3	1	6	10
	0.5	0	4	7	11
	2.0	0	7	2	9
FOCUS - DARK, VARIOUS LOCATORS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	2	0	2
PITUITARY					
NO LESIONS RECOGNIZED.	0	2	4	23	29
	0.01	1	6	18	25
	0.1	4	2	24	30
	0.5	3	7	16	26
	2.0	4	12	13	29
CYST, FOCAL OR MULTIFOCAL:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	1	0	1	2
	0.5	0	0	0	0
	2.0	0	0	0	0
INCREASED SIZE - SLIGHT:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
PITUITARY (CONTINUED)					
FOCUS - DARK:	0	0	0	18	18
	0.01	0	1	12	13
	0.1	0	1	7	8
	0.5	1	1	10	12
	2.0	0	6	3	9
MASS / NODULE:	0	0	4	9	13
	0.01	1	3	18	22
	0.1	3	2	15	20
	0.5	0	5	16	21
	2.0	0	10	13	23
SPINAL CORD NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
PERIPHERAL NERVE NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
PANCREAS NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
BONE NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	46	59
	0.5	4	13	43	60
	2.0	4	28	29	61
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
ADRENAL					
NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	9	48	59
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	25	29	58
INCREASED SIZE, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
FOCUS - DARK, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
FOCUS - PALE, UNILATERAL:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
KIDNEY					
NO LESIONS RECOGNIZED.	0	2	7	40	49
	0.01	2	8	33	43
	0.1	7	5	33	45
	0.5	4	5	27	36
	2.0	3	25	20	48
DILATED, PELVIS, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
DILATED, PELVIS, BILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
FIBROSIS, CAPSULE, UNILATERAL, FOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
KIDNEY (CONTINUED)					
DARK, VARIOUS DESCRIPTORS:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	1	0	1	2
	0.5	0	3	0	3
	2.0	0	2	0	2
FOCUS - PALE, CORTEX, BILATERAL, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
PALE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
ROUGHENED SURFACE - UNSPECIFIED DEGREE:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	1	0	1
ROUGHENED SURFACE - SLIGHT:	0	0	1	8	9
	0.01	0	0	13	13
	0.1	0	0	11	11
	0.5	0	2	15	17
	2.0	0	0	7	7
ROUGHENED SURFACE - MODERATE:	0	0	0	2	2
	0.01	0	0	2	2
	0.1	0	0	1	1
	0.5	0	0	1	1
	2.0	0	0	0	0
ROUGHENED SURFACE - SEVERE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
ORAL CAVITY					
NO LESIONS RECOGNIZED.	0	1	8	49	58
	0.01	2	10	46	58
	0.1	8	5	45	58
	0.5	3	13	42	58
	2.0	4	25	25	54
OVERGROWN INCISORS:	0	1	0	1	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
ROUGH, ELEVATED OR VERRUCOUS-LIKE LESION, HARD PALATE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	1	0	1	2
	2.0	0	1	3	4
MALOCCLUSION:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	2	2
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	1	1	2
TONGUE					
NO LESIONS RECOGNIZED.	0	2	8	49	59
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	27	28	59
MASS / NODULE:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	1	2
ESOPHAGUS					
NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
STOMACH					
NO LESIONS RECOGNIZED.	0	2	3	50	55
	0.01	2	5	45	52
	0.1	7	4	46	57
	0.5	1	6	41	48
	2.0	3	19	26	48
HEMORRHAGE, GLANDULAR WALL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
ULCER AND/OR EROSION, GLANDULAR MUCOSA:	0	0	1	0	1
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
ULCER AND/OR EROSION, GLANDULAR MUCOSA, MULTIFOCAL:	0	0	2	0	2
	0.01	0	3	1	4
	0.1	1	0	1	2
	0.5	0	3	0	3
	2.0	1	4	0	5
ULCER AND/OR EROSION, NONGLANDULAR MUCOSA:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	1	1	1	3
	2.0	0	1	1	2
ULCER AND/OR EROSION, NONGLANDULAR MUCOSA, MULTIFOCAL:	0	0	1	0	1
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	2	0	2
	2.0	0	0	0	0
DECREASED INGESTA:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	2	0	2
	2.0	0	2	0	2
FOCUS - DARK, VARIOUS LOCATORS, FOCAL OR MULTIFOCAL:	0	0	2	0	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	2	0	2
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
STOMACH (CONTINUED)					
FOCUS - ELEVATED, GLANDULAR MUCOSA:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
HEMOLYZED BLOOD, VARIOUS LOCATORS:	0	0	0	0	0
	0.01	0	0	2	2
	0.1	1	1	0	2
	0.5	1	1	0	2
	2.0	0	3	1	4
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	1	0	1	2
	2.0	0	0	1	1
SMALL INTESTINE NO LESIONS RECOGNIZED.	0	2	7	50	59
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	3	11	42	56
	2.0	4	24	28	56
EDEMA, DUODENUM WALL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
DECREASED INGESTA:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	1	2	0	3
	2.0	0	2	0	2
GAS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	1	0	0	1
	2.0	0	0	0	0
HEMOLYZED BLOOD:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1

[a] Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
SMALL INTESTINE (CONTINUED)					
INCREASED SIZE - PROBABLY LYMPHORETICULAR TUMOR, PEYER'S PATCH:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	0	0
CECUM NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	4	47	59
	0.5	4	11	43	58
	2.0	4	27	28	59
EDEMA, WALL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
DECREASED INGESTA:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
ULCER - PERFORATED, MUCOSA, FOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	1	1
COLON NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
RECTUM					
NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	9	48	59
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
ABSCESS, SEROSA:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
URINARY BLADDER					
NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	11	43	58
	2.0	3	27	28	58
CALCULUS(I) AND/OR STONE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	1	0	1	2
HEMORRHAGE, MUCOSA:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	1	0	1
THICKENED, WALL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
URETER					
NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
URETHRA					
NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
OVARY					
NO LESIONS RECOGNIZED.	0	1	7	46	54
	0.01	1	10	44	55
	0.1	6	5	41	52
	0.5	4	13	40	57
	2.0	4	27	25	56
INCREASED SIZE, BILATERAL:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
CYST - DARK, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
DISTENDED - WITH CLEAR FLUID, OVARIAN BURSA, UNILATERAL:	0	1	1	4	6
	0.01	0	0	4	4
	0.1	1	0	6	7
	0.5	0	0	2	2
	2.0	0	0	2	2
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	1	2	3
OVIDUCT					
NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	46	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
UTERUS					
NO LESIONS RECOGNIZED.	0	2	7	27	36
	0.01	1	7	27	35
	0.1	7	3	32	42
	0.5	2	7	31	40
	2.0	3	17	13	33

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
UTERUS (CONTINUED)					
HEMORRHAGE, LUMEN:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
HYPERPLASIA - CYSTIC ENDOMETRIAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
INTUSSUSCEPTION, LEFT HORN:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	1	0	0	1
	2.0	0	0	0	0
CYST - CLEAR, WALL, UNILATERAL:	0	0	1	0	1
	0.01	0	0	3	3
	0.1	0	0	1	1
	0.5	0	0	3	3
	2.0	0	0	1	1
CYST - CLEAR, WALL, UNILATERAL, MULTIFOCAL:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
DISTENDED - WITH CLEAR FLUID:	0	0	0	0	0
	0.01	0	0	3	3
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	1	1	2
EXUDATE - CLOUDY OR MUCOID:	0	0	0	2	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
MASS / NODULE:	0	0	0	16	16
	0.01	1	3	11	15
	0.1	1	2	14	17
	0.5	2	5	7	14
	2.0	1	5	7	13

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
UTERUS (CONTINUED)					
MASS / NODULE, (TWO):	0	0	0	4	4
	0.01	0	0	6	6
	0.1	0	0	0	0
	0.5	0	1	3	4
	2.0	0	4	5	9
MASS / NODULE, (THREE):	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
MASS / NODULE, (FOUR):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
CERVIX NO LESIONS RECOGNIZED.	0	2	8	49	59
	0.01	2	9	47	58
	0.1	6	5	46	57
	0.5	4	13	42	59
	2.0	4	28	27	59
THICKENED:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	1	1
MASS / NODULE:	0	0	0	1	1
	0.01	0	1	1	2
	0.1	2	0	0	2
	0.5	0	0	1	1
	2.0	0	0	1	1
VAGINA NO LESIONS RECOGNIZED.	0	2	8	49	59
	0.01	2	8	48	58
	0.1	8	5	47	60
	0.5	3	13	42	58
	2.0	4	24	28	56
HEMORRHAGE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	1	1

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
VAGINA (CONTINUED)					
DISTENDED - WITH CLOUDY OR MUCOID FLUID:	0	0	0	0	0
	0.01	0	2	0	2
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	4	0	4
MASS / NODULE:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	1	0	0	1
	2.0	0	0	0	0
LUNGS NO LESIONS RECOGNIZED.	0	1	5	48	54
	0.01	2	8	46	56
	0.1	7	4	46	57
	0.5	3	10	41	54
	2.0	4	24	29	57
ATELECTASIS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	1	0	1
CONGESTION:	0	0	1	0	1
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	1	0	1
AREA - DARK, ONE LOBE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - DARK, VARIOUS LOCATORS AND GRADES, MULTIFOCAL:	0	1	2	0	3
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	2	0	2
	2.0	0	2	0	2
FOCUS - DARK DEPRESSED, ONE LOBE:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
LUNGS (CONTINUED)					
FOCUS - DARK ELEVATED, ONE LOBE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	1	0	0	1
	2.0	0	0	0	0
FOCUS - PALE, ONE LOBE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
PETECHIA, MULTIFOCAL:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
ASPIRATED BLOOD - SECONDARY TO DECAPITATION:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	1	1
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	2	2
	2.0	0	0	0	0
LARYNX NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
TRACHEA NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
SKELETAL MUSCLE NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	26	29	59

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
SKELETAL MUSCLE (CONTINUED)					
HEMORRHAGE, THORAX, MULTIFOCAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
SALIVARY GLAND NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
THYMUS NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	1	10	48	59
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
INCREASED SIZE - PROBABLY LYMPHORETICULAR TUMOR:	0	0	0	0	0
	0.01	1	0	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
AORTA NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
THYROID GLAND NO LESIONS RECOGNIZED.	0	2	8	49	59
	0.01	2	8	47	57
	0.1	8	5	47	60
	0.5	4	13	42	59
	2.0	4	28	28	60

[a] Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
THYROID GLAND (CONTINUED)					
INCREASED SIZE, UNILATERAL:	0	0	0	1	1
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
FOCUS - DARK, UNILATERAL:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	1	1
	2.0	0	0	1	1
PARATHYROID GLAND NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	12	43	59
	2.0	4	28	29	61
HYPERPLASIA:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
MAMMARY GLAND NO LESIONS RECOGNIZED.	0	2	4	41	47
	0.01	2	7	37	46
	0.1	7	5	37	49
	0.5	4	6	27	37
	2.0	4	16	17	37
GALACTOCELE:	0	0	0	2	2
	0.01	0	1	2	3
	0.1	0	0	2	2
	0.5	0	0	5	5
	2.0	0	0	1	1

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	50
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
MAMMARY GLAND (CONTINUED)					
GALACTOCELE, (TWO):	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
GALACTOCELE, (THREE):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
HYPERPLASIA, DIFFUSE:	0	0	3	0	3
	0.01	0	1	0	1
	0.1	1	0	0	1
	0.5	0	3	2	5
	2.0	0	3	0	3
MASS / NODULE:	0	0	1	5	6
	0.01	0	1	10	11
	0.1	0	0	8	8
	0.5	0	3	11	14
	2.0	0	8	8	16
MASS / NODULE, (TWO):	0	0	0	2	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	2	1	3
	2.0	0	1	1	2
MASS / NODULE, (THREE):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	1	1
MASS / NODULE, (FOUR):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	1	0	1
	2.0	0	0	0	0
EYE NO LESIONS RECOGNIZED.	0	2	8	48	58
	0.01	2	9	43	54
	0.1	8	4	43	55
	0.5	4	12	39	55
	2.0	3	27	27	57

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
EYE (CONTINUED)					
ATROPHY, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	0	1
INCREASED SIZE, UNILATERAL:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	1	0	1
CLOUDY, CORNEA, UNILATERAL:	0	0	0	1	1
	0.01	0	0	0	0
	0.1	0	1	1	2
	0.5	0	1	1	2
	2.0	0	0	1	1
OPACITY, LENS, UNILATERAL, DIFFUSE: - SEVERE	0	0	0	1	1
	0.01	0	1	3	4
	0.1	0	0	2	2
	0.5	0	0	3	3
	2.0	1	0	1	2
OPACITY, LENS, BILATERAL, DIFFUSE: - SEVERE	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	1	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	0
NASAL TURBINATES NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
LACRIMAL GLAND NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	27	29	60

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
LACRIMAL GLAND (CONTINUED)					
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
ZYMBAL GLAND NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	27	29	60
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
ABDOMINAL CAVITY NO LESIONS RECOGNIZED.	0	1	5	43	49
	0.01	2	9	45	56
	0.1	4	4	37	45
	0.5	0	6	37	43
	2.0	2	17	21	40
ADHESIONS - FIBRINOUS OR FIBROUS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	2	1	3
	2.0	0	0	1	1
ASCITES - SEROSANGUINEOUS:	0	0	1	0	1
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	1	2
FAT - DECREASED AMOUNT, VARIOUS GRADES:	0	1	1	3	5
	0.01	0	0	1	1
	0.1	0	1	2	3
	0.5	3	5	0	8
	2.0	0	7	2	9
FAT - STRANGULATED OR NECROTIC PORTION:	0	0	1	4	5
	0.01	0	0	2	2
	0.1	3	0	6	9
	0.5	0	0	5	5
	2.0	1	2	4	7

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
ABDOMINAL CAVITY (CONTINUED)					
INFLAMMATION - PURULENT, DIFFUSE - MODERATE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
ACCESSORY SPLEEN:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	2	2
	0.5	1	0	0	1
	2.0	0	0	0	0
HEMOPERITONEUM OR BLOOD:	0	0	0	0	0
	0.01	0	1	0	1
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	1	0	2
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	1	2
LYMPH NODES NO LESIONS RECOGNIZED.	0	2	8	49	59
	0.01	1	9	47	57
	0.1	7	3	47	57
	0.5	3	10	43	56
	2.0	4	24	26	54
INCREASED SIZE, ONE OR MORE INDIVIDUAL LYMPH NODES:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	1	2	0	3
	2.0	0	1	1	2
INCREASED SIZE - PROBABLY LYMPHORETICULAR TUMOR, ONE OR MORE INDIVIDUAL LYMPH NODES:	0	0	0	1	1
	0.01	1	1	1	3
	0.1	1	1	0	2
	0.5	0	1	0	1
	2.0	0	3	0	3
INCREASED PIGMENT, ONE OR MORE INDIVIDUAL LYMPH NODES:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0

[a]Data presented as the number of animals with the stated observation.

TABLE 22 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Gross Pathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-24 MONTHS	TERMINAL KILL	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61
LYMPH NODES (CONTINUED)					
MASS / NODULE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	2	2
THORACIC CAVITY NO LESIONS RECOGNIZED.	0	2	6	45	53
	0.01	2	10	46	58
	0.1	7	4	46	57
	0.5	4	13	43	60
	2.0	4	25	29	58
HYDROTHORAX - CLEAR:	0	0	2	0	2
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	1	0	1
HYDROTHORAX - CLOUDY:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	1	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
HYDROTHORAX - SEROSANGUINEOUS:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	2	0	2
INFLAMMATION - PURULENT, PLEURAL CAVITY, DIFFUSE - SEVERE:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	1	0	0	1
	0.5	0	0	0	0
	2.0	0	0	0	0
HEMORRHAGE - TERMINAL:	0	0	0	5	5
	0.01	0	0	2	2
	0.1	0	0	1	1
	0.5	0	0	0	0
	2.0	0	0	0	0
VASCULATURE NO LESIONS RECOGNIZED.	0	2	8	50	60
	0.01	2	10	48	60
	0.1	8	5	47	60
	0.5	4	13	43	60
	2.0	4	28	29	61

[a]Data presented as the number of animals with the stated observation.

TABLE 23

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
PERIPHERAL NERVE, TIBIAL						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	0	0	1	2
	0.01	2	0	0	1	3
	0.1	0	1	1	2	4
	0.5	2	0	0	1	3
	2.0	2	0	1	1	4
DEGENERATION - VERY SLIGHT:	0	0	2	6	22	30
	0.01	5	3	1	20	29
	0.1	1	0	7	15	23
	0.5	0	3	6	16	25
	2.0	2	0	11	6	19
DEGENERATION - SLIGHT:	0	0	0	5	14	19
	0.01	0	0	2	20	22
	0.1	1	0	3	17	21
	0.5	0	2	2	15	19
	2.0	0	2	3	16	21
DEGENERATION - MODERATE:	0	0	0	2	6	8
	0.01	0	0	0	5	5
	0.1	0	0	0	12	12
	0.5	0	0	1	12	13
	2.0	0	0	1	11	12
DEGENERATION - SEVERE:	0	0	0	0	1	1[b] T t
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	3	1	4
TOTAL RATS WITH DEGENERATION - ANY GRADE	0	0	2	13	43	58
	0.01	5	3	3	46	57
	0.1	2	0	10	44	56
	0.5	0	5	9	43	57
	2.0	2	2	18	34	56
PERIPHERAL NERVE, SAPHENOUS						
NUMBER OF TISSUES EXAMINED	0	0	0	0	10	10
	0.01	0	0	0	10	10
	0.1	0	0	0	10	10
	0.5	0	0	0	10	10
	2.0	0	0	0	10	10

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

T INDICATES A LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, $\alpha=0.05$.

t INDICATES A LINEAR TREND BY MANTEL-HAENSZEL EXTENSION OF THE COCHRAN-ARMITAGE TEST (PETO), $\alpha=0.05$.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
PERIPHERAL NERVE, SAPHENOUS (CONTINUED)						
WITHIN NORMAL LIMITS:	0	-	-	-	10	10
	0.01	-	-	-	10	10
	0.1	-	-	-	9	9
	0.5	-	-	-	9	9
	2.0	-	-	-	5	5
DEGENERATION - VERY SLIGHT	0	-	-	-	0	0
	0.01	-	-	-	0	0
	0.1	-	-	-	1	1
	0.5	-	-	-	1	1
	2.0	-	-	-	5	5*
PERIPHERAL NERVE, BRACHIAL PLEXUS						
NUMBER OF TISSUES EXAMINED	0	0	0	0	10	10
	0.01	0	0	0	10	10
	0.1	0	0	0	10	10
	0.5	0	0	0	10	10
	2.0	0	0	0	10	10
WITHIN NORMAL LIMITS:	0	-	-	-	7	7
	0.01	-	-	-	7	7
	0.1	-	-	-	4	4
	0.5	-	-	-	2	2
	2.0	-	-	-	4	4
DEGENERATION - VERY SLIGHT:	0	-	-	-	3	3
	0.01	-	-	-	2	2
	0.1	-	-	-	6	6
	0.5	-	-	-	8	8
	2.0	-	-	-	5	5
DEGENERATION - SLIGHT:	0	-	-	-	0	0
	0.01	-	-	-	1	1
	0.1	-	-	-	0	0
	0.5	-	-	-	0	0
	2.0	-	-	-	1	1
TOTAL RATS WITH DEGENERATION - ANY GRADE	0	-	-	-	3	3T
	0.01	-	-	-	3	3
	0.1	-	-	-	6	6
	0.5	-	-	-	8	8
	2.0	-	-	-	6	6

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION. - INDICATES NOT APPLICABLE.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0.05.
T INDICATES A LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, α = 0.05..

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
PERIPHERAL NERVE, TRIGEMINAL						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	13	41	57
	0.01	7	3	3	44	57
	0.1	2	1	11	44	58
	0.5	2	5	9	42	58
	2.0	4	2	19	30	55
DEGENERATION, UNILATERAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION - SECONDARY TO ORBITAL BLEEDING, UNILATERAL - SLIGHT:	0	0	0	0	2	2
	0.01	0	0	0	2	2
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
DEGENERATION - SECONDARY TO ORBITAL BLEEDING, UNILATERAL - MODERATE:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
DEGENERATION - SECONDARY TO ORBITAL BLEEDING, UNILATERAL - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	3	3
BRAIN						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	0	2	9	36	47
	0.01	6	3	2	42	53
	0.1	1	1	10	38	50
	0.5	1	5	8	38	52
	2.0	3	1	15	30	49

[a]DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
BRAIN (CONTINUED)						
ASTROCYTOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	3	3
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	0	1	2
	2.0	0	0	1	1	2
OLIGODENDROGLIOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	1	0	0	1	2
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
ADENOCARCINOMA, (PITUITARY), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
GLIAL PROLIFERATION (SUGGESTIVE OF EARLY TUMOR), FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	1	1
DEGENERATION, FOCAL - VERY SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION, OPTIC NERVE OR TRACT, UNILATERAL - MODERATE:	0	0	0	0	1	1
	0.01	0	0	0	2	2
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	1	0	1	1	3
DEGENERATION, OPTIC NERVE OR TRACT, UNILATERAL - SEVERE:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION, OPTIC NERVE OR TRACT, BILATERAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
BRAIN (CONTINUED)						
GLIOSIS, FOCAL - VERY SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
MALACIA, FOCAL - SLIGHT:	0	0	0	2	0	2
	0.01	0	0	1	0	1
	0.1	1	0	0	1	2
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
MINERALIZATION, FOCAL - VERY SLIGHT OR SLIGHT:	0	0	0	1	1	2
	0.01	0	0	0	0	0
	0.1	0	0	0	4	4
	0.5	0	0	0	2	2
	2.0	0	0	1	1	2
PERIVASCULAR MONONUCLEAR (LYMPHOID) CELL CUFFING, FOCAL OR MULTIFOCAL- VERY SLIGHT:	0	0	0	0	2	2
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	1	1	0	0	2
THROMBUS - CHRONIC OR ORGANIZED, FOCAL:	0	1	0	1	0	2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SPINAL CORD, CERVICAL REGION						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	1	8	24	34
	0.01	4	3	3	35	45
	0.1	2	1	5	28	36
	0.5	0	5	8	22	35
	2.0	3	2	13	20	38
ASTROCYTOMA, GRAY MATTER, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	2	2

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SPINAL CORD, CERVICAL REGION (CONTINUED)						
UNDIFFERENTIATED GLIAL CELL TUMOR, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.1	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION, WHITE MATTER - VERY SLIGHT:	0	0	0	4	17	21
	0.01	3	0	0	12	15
	0.1	0	0	6	17	23
	0.5	2	0	1	20	23
	2.0	0	0	6	14	20
DEGENERATION, WHITE MATTER - SLIGHT:	0	0	1	0	2	3
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	2	2
	2.0	1	0	0	0	1
TOTAL RATS WITH DEGENERATION, WHITE MATTER - ANY GRADE:	0	0	1	4	19	24
	0.01	3	0	0	12	15
	0.1	0	0	6	18	24
	0.5	2	0	1	22	25
	2.0	1	0	6	14	21
INFLAMMATION - SUPPURATIVE, MENINGES, FOCAL - MODERATE:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SPINAL CORD, THORACIC REGION						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	1	6	26	34
	0.01	6	1	2	32	41
	0.1	1	1	8	26	36
	0.5	2	5	7	22	36
	2.0	4	0	12	16	32
ASTROCYTOMA, GRAY MATTER, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	0	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SPINAL CORD, THORACIC REGION (CONTINUED)						
DEGENERATION, WHITE MATTER - VERY SLIGHT:	0	0	0	7	15	22
	0.01	1	2	1	14	18
	0.1	1	0	3	19	23
	0.5	0	0	2	17	19
	2.0	0	1	7	16	24
DEGENERATION, WHITE MATTER - SLIGHT:	0	0	0	0	3	3
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	5	5
	2.0	0	1	0	3	4
TOTAL RATS WITH DEGENERATION, WHITE MATTER - ANY GRADE:	0	0	0	7	18	25
	0.01	1	2	1	15	19
	0.1	1	0	3	20	24
	0.5	0	0	2	22	24
	2.0	0	2	7	19	28
GLIOSIS, WHITE MATTER, FOCAL - MODERATE:	0	0	1	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SPINAL CORD, LUMBOSACRAL REGION						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	0	6	16	23
	0.01	6	2	0	15	23
	0.1	1	1	7	12	21
	0.5	2	4	7	17	30
	2.0	3	0	14	17	34
ASTROCYTOMA, GRAY MATTER, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
GLIAL PROLIFERATION (SUGGESTIVE OF EARLY TUMOR), GRAY MATTER, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SPINAL CORD, LUMBOSACRAL REGION (CONTINUED)						
DEGENERATION, WHITE MATTER - VERY SLIGHT:	0	0	2	6	22	30
	0.01	0	0	3	25	28
	0.1	0	0	3	29	32
	0.5	0	1	2	21	24
	2.0	0	1	4	13	18
DEGENERATION, WHITE MATTER - SLIGHT:	0	0	0	1	6	7
	0.01	1	1	0	7	9
	0.1	1	0	1	5	7
	0.5	0	0	0	6	6
	2.0	0	0	0	5	5
TOTAL RATS WITH DEGENERATION, WHITE MATTER - ANY GRADE:	0	0	2	7	28	37
	0.01	1	1	3	32	37
	0.1	1	0	4	34	39
	0.5	0	1	2	27	30
	2.0	0	1	4	18	23*
EPIDERMOID CYST, MENINGES, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	1	1	0	3
LIVER						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	0	0	0	0	0
	0.01	0	1	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
CARCINOMA, HEPATOCELLULAR, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	2	2
HYPERPLASTIC (NEOPLASTIC) NODULE, HEPATOCELLULAR, BENIGN, PRIMARY:	0	0	0	0	2	2
	0.01	0	0	0	2	2
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, $\alpha=0.05$.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
LIVER (CONTINUED)						
ABSCESS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
ACCENTUATED LOBULAR PATTERN:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, MULTIFOCAL - SLIGHT:	0	0	1	0	13	14
	0.01	0	0	0	16	16
	0.1	0	0	1	14	15
	0.5	1	0	0	9	10
	2.0	0	0	2	9	11
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, MULTIFOCAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
ARCHITECTURE ALTERED SECONDARY TO DIAPHRAGMATIC HERNIA:	0	0	0	1	1	-2
	0.01	0	0	0	2	2
	0.1	0	1	1	2	4
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
AREA(S) OF ALTERED CELLS, HEPATOCELLULAR, ONE:	0	0	0	2	17	19
	0.01	1	0	0	8	9
	0.1	0	0	2	14	16
	0.5	0	0	1	11	12
	2.0	0	1	6	5	12
AREA(S) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL (TWO TO FOUR):	0	0	0	1	8	9
	0.01	0	0	0	15	15
	0.1	0	0	2	12	14
	0.5	0	0	0	11	11
	2.0	0	0	3	17	20
AREA(S) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL (FIVE OR MORE):	0	0	0	0	0	0[b]
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1*M

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, $\alpha=0.05$.

M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), $\alpha=0.05$.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
LIVER (CONTINUED)						
TOTAL RATS WITH ONE OR MORE AREAS OF ALTERED CELLS:	0	0	0	3	25	28
	0.01	1	0	0	23	24
	0.1	0	0	4	27	31
	0.5	0	0	1	23	24
	2.0	0	1	9	23	33
CYSTIC DILATATION, BILE DUCT(S), FOCAL:	0	0	0	1	0	1
	0.01	0	0	0	3	3
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION - CYSTIC, FOCAL OR MULTIFOCAL:	0	0	0	4	17	21
	0.01	0	1	1	20	22
	0.1	0	0	4	16	20
	0.5	0	0	1	24	25
	2.0	1	0	7	17	25
FIBROSIS, CAPSULE, MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
FOCUS(I) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL (ONE TO FIVE):	0	1	0	4	4	-9
	0.01	2	1	1	2	6
	0.1	2	1	3	2	8
	0.5	0	1	1	2	4
	2.0	1	1	11	3	16
FOCUS(I) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL (SIX TO FIFTEEN):	0	0	2	4	23	29
	0.01	1	0	0	20	21
	0.1	0	0	4	22	26
	0.5	0	4	2	19	25
	2.0	0	0	5	17	22
FOCUS(I) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL (SIXTEEN OR MORE):	0	0	0	0	17	17
	0.01	0	0	1	24	25
	0.1	0	0	1	21	22
	0.5	0	0	2	23	25
	2.0	0	1	1	15	17
TOTAL RATS WITH ONE OR MORE FOCI OF ALTERED CELLS:	0	1	2	8	44	55
	0.01	3	1	2	46	52
	0.1	2	1	8	45	56
	0.5	0	5	5	44	54
	2.0	1	2	17	35	55

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
LIVER (CONTINUED)						
GRANULOMA(S) - MICRO, MULTIFOCAL:	0	0	0	0	4	4
	0.01	0	0	0	5	5
	0.1	0	0	0	4	4
	0.5	0	1	0	4	5
	2.0	0	0	0	2	2
HYPERPLASIA, BILE DUCT(S), MULTIFOCAL - VERY SLIGHT:	0	0	1	1	6	8
	0.01	2	0	0	7	9
	0.1	1	0	4	8	13
	0.5	1	1	3	3	8
	2.0	0	2	6	3	11
HYPERPLASIA, BILE DUCT(S), MULTIFOCAL - SLIGHT:	0	0	1	9	32	42
	0.01	5	1	3	29	38
	0.1	1	1	4	31	37
	0.5	1	4	3	34	42
	2.0	0	0	12	31	43
HYPERPLASIA, BILE DUCT(S), MULTIFOCAL - MODERATE:	0	0	0	3	6	9
	0.01	0	1	0	11	12
	0.1	0	0	2	7	9
	0.5	0	0	3	7	10
	2.0	2	0	0	1	3
TOTAL RATS WITH BILIARY HYPERPLASIA OF ANY DEGREE:	0	0	2	13	44	59
	0.01	7	2	3	47	59
	0.1	2	1	10	46	59
	0.5	2	5	9	44	60
	2.0	2	2	18	35	57
INFARCT, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, PERIPORTAL, MULTIFOCAL - VERY SLIGHT:	0	0	2	4	13	19
	0.01	3	0	0	12	15
	0.1	0	0	4	13	17
	0.5	0	2	3	14	19
	2.0	0	1	5	10	16
INFLAMMATION - CHRONIC, PERIPORTAL, MULTIFOCAL - SLIGHT:	0	0	0	1	30	31
	0.01	1	0	0	32	33
	0.1	0	1	1	28	30
	0.5	1	0	2	29	32
	2.0	1	0	2	22	25

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
LIVER (CONTINUED)						
TOTAL RATS WITH INFLAMMATION - CHRONIC, PERIPORTAL, ANY DEGREE:	0	0	2	5	43	50
	0.01	4	0	0	44	48
	0.1	0	1	5	41	47
	0.5	1	2	5	43	51
	2.0	1	1	7	32	41
NECROSIS, CENTRILOBULAR - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	2	0	2
	2.0	0	0	1	0	1
NECROSIS, CENTRILOBULAR - MODERATE:	0	0	0	2	0	2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	3	0	3
	2.0	1	0	2	0	3
NECROSIS, CENTRILOBULAR - SEVERE:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
VACUOLIZATION CONSISTENT WITH FATTY CHANGE, HEPATOCELLULAR - SLIGHT:	0	0	0	0	8	-8
	0.01	1	0	0	9	10
	0.1	1	0	2	7	10
	0.5	1	1	0	7	9
	2.0	0	0	5	3	8
VACUOLIZATION CONSISTENT WITH FATTY CHANGE, HEPATOCELLULAR - MODERATE:	0	0	0	1	0	1
	0.01	1	0	1	2	4
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
THROMBUS - CHRONIC OR ORGANIZED, FOCAL OR MULTIFOCAL:	0	0	0	1	0	1
	0.01	1	0	0	0	1
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
NECROSIS WITH ACCOMPANYING INFLAMMATION, FOCAL OR MULTIFOCAL- SLIGHT:	0	0	0	4	2	6
	0.01	1	0	0	5	6
	0.1	0	0	0	1	1
	0.5	0	0	0	7	7
	2.0	1	0	2	2	5

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
HEART						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	0	1	27	29
	0.01	4	2	0	19	25
	0.1	1	1	5	18	25
	0.5	1	3	8	16	28
	2.0	2	1	8	12	23
CARCINOMA, (LUNG), MALIGNANT, SECONDARY:	0	0	1	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CYST, A/V VALVE, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
DEGENERATION WITH OR WITHOUT INFLAMMATION, MYOCARDIUM, MULTIFOCAL - SLIGHT:	0	0	1	11	15	27
	0.01	3	1	3	27	34
	0.1	1	0	6	25	32
	0.5	1	2	1	27	31
	2.0	0	1	11	22	34
DEGENERATION WITH OR WITHOUT INFLAMMATION, MYOCARDIUM, MULTIFOCAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	1	0	0	1	2
DEGENERATION WITH OR WITHOUT INFLAMMATION, MYOCARDIUM, MULTIFOCAL - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
DEGENERATION WITH OR WITHOUT INFLAMMATION, MYOCARDIUM, MULTIFOCAL - ANY DEGREE:	0	0	1	11	15	27
	0.01	3	1	3	28	35M
	0.1	1	0	6	25	32
	0.5	1	2	1	28	32
	2.0	2	1	11	23	37

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
HEART (CONTINUED)						
THROMBUS - CHRONIC OR ORGANIZED, ATRIUM:	0	0	0	2	0	2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	1	0	1
DEGENERATION AND FIBROSIS, MYOCARDIUM, FOCAL OR MULTIFOCAL - MODERATE:	0	0	0	0	3	3
	0.01	0	0	0	1	1
	0.1	0	0	0	3	3
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SPLEEN						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	0	1	3	30	34
	0.01	4	0	0	34	38
	0.1	0	1	4	31	36
	0.5	2	2	2	29	35
	2.0	2	0	5	21	28
HEMANGIOSARCOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
HISTIOCYTIC SARCOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	0	0	1
LEUKEMIA - FISCHER RAT, MALIGNANT, PRIMARY, METASTASIS, MULTIPLE ORGANS:	0	0	0	6	4	10
	0.01	3	3	3	11	20
	0.1	1	0	5	8	14
	0.5	0	2	4	8	14
	2.0	1	0	6	9	16
CYST, CAPSULE, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
FIBROSIS, FOCAL:	0	0	0	0	1	1Tt
	0.01	0	0	0	1	1
	0.1	0	0	0	2	2
	0.5	0	0	0	3	3
	2.0	0	0	1	3	4

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
T INDICATES A LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, α=0.05.
t INDICATES A LINEAR TREND BY MANTEL-HAENSZEL EXTENSION OF THE COCHRAN-ARMITAGE TEST (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SPLEEN (CONTINUED)						
FIBROSIS, CAPSULE, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
GRANULOMA(S) - MICRO, MULTIFOCAL:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFARCT, FOCAL:	0	0	0	1	0	1
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
INFARCT, DIFFUSE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
PIGMENT - HEMATOGENOUS - INCREASED - MODERATE:	0	0	0	1	1	-2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	0	1
	2.0	0	1	0	0	1
EXTRAMEDULLARY HEMATOPOIESIS--INCREASED - SLIGHT:	0	0	0	1	4	5
	0.01	0	0	0	2	2
	0.1	0	0	1	5	6
	0.5	0	0	1	4	5
	2.0	0	0	3	1	4
EXTRAMEDULLARY HEMATOPOIESIS--INCREASED - MODERATE:	0	1	1	0	1	3
	0.01	0	0	0	0	0
	0.1	1	0	1	0	2
	0.5	0	0	2	0	2
	2.0	0	0	4	2	6
EXTRAMEDULLARY HEMATOPOIESIS--INCREASED - SEVERE:	0	0	0	2	0	2
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	1	0	0	1	2
TOTAL RATS WITH EXTRAMEDULLARY HEMATOPOIESIS--INCREASED - ANY GRADE:	0	1	1	3	5	10
	0.01	0	0	0	2	2M
	0.1	1	0	2	6	9
	0.5	0	0	3	5	8
	2.0	1	0	7	4	12

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
PITUITARY						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	6	3	3	47	59
	0.1	2	1	10	45	58
	0.5	2	5	7	43	57
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	1	6	18	26
	0.01	6	3	1	18	28
	0.1	1	1	4	16	22
	0.5	1	4	5	23	33
	2.0	4	1	8	20	33
ADENOCARCINOMA, ANTERIOR (PARS DISTALIS), MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	3	3
	2.0	0	0	1	1	2
ADENOMA, ANTERIOR (PARS DISTALIS), BENIGN, PRIMARY:	0	0	0	5	17	22
	0.01	0	0	2	13	15
	0.1	0	0	2	21	23
	0.5	1	0	1	10	12
	2.0	0	0	7	10	17
CYST, ANTERIOR (PARS DISTALIS), FOCAL:	0	0	0	0	3	-3
	0.01	0	0	0	5	5
	0.1	1	0	1	4	6
	0.5	0	0	1	4	5
	2.0	0	0	1	1	2
DILATED, SINUSOIDS:	0	0	0	1	2	3
	0.01	0	0	0	5	5
	0.1	0	0	0	3	3
	0.5	0	0	0	2	2
	2.0	0	1	1	2	4
HEMATOCYST (HEMATOMA):	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	0	1
	2.0	0	0	0	0	0
HYPERPLASIA, ANTERIOR (PARS DISTALIS), FOCAL:	0	0	1	2	4	7
	0.01	0	0	0	7	7
	0.1	0	0	2	6	8
	0.5	0	0	0	4	4
	2.0	0	0	1	2	3

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
PITUITARY (CONTINUED)						
HYPERPLASIA - ADENOMATOUS, PARS INTERMEDIA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
NECROSIS, ANTERIOR (PARS DISTALIS), FOCAL OR MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	1	0	1
INFLAMMATION - SUBACUTE TO CHRONIC, PARS INTERMEDIA, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
PANCREAS						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	3	2	19	35	59
WITHIN NORMAL LIMITS:	0	1	1	4	15	21
	0.01	3	2	2	15	22
	0.1	1	1	1	12	15
	0.5	2	3	3	13	21
	2.0	2	1	6	7	16
ADENOCARCINOMA, ISLETS, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ADENOMA, ACINI, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
ADENOMA, ISLETS, BENIGN, PRIMARY:	0	0	0	3	6	9
	0.01	1	1	0	10	12
	0.1	0	0	4	10	14
	0.5	0	0	3	10	13
	2.0	0	1	4	5	10
ADENOMA, ISLETS, BENIGN, PRIMARY, (TWO):	0	0	0	0	2	2[c]
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	3	3

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[c] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH THE DATA FROM RATS HAVING ONLY ONE ADENOMA. ANY INDICATED SIGNIFICANCE IN THIS DIAGNOSTIC CATEGORY IS FOR THE COMBINED VALUES.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
PANCREAS (CONTINUED)						
ATROPHY, ACINI, FOCAL OR MULTIFOCAL - SLIGHT:	0	0	1	3	18	22
	0.01	3	0	0	22	25
	0.1	1	0	7	18	26
	0.5	0	2	3	21	26
	2.0	0	0	7	15	22
ATROPHY, ACINI, FOCAL OR MULTIFOCAL - MODERATE:	0	0	0	0	4	4
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	1	1	2
ATROPHY, ACINI, DIFFUSE - SEVERE:	0	0	0	1	2	3
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DILATATION, DUCTS, FOCAL OR MULTIFOCAL:	0	0	0	1	2	3
	0.01	0	0	0	6	6
	0.1	0	0	4	4	8M
	0.5	0	0	1	3	4
	2.0	0	0	1	1	2
FOCUS(I) OF ALTERED CELLS - BASOPHILIC, ACINI, FOCAL:	0	0	0	1	1	-2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	0	0	0	0
HEMATOCYST (HEMATOMA), FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
HYPERPLASIA, ISLETS, FOCAL:	0	0	0	0	2	2
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	0	2	2
	2.0	1	0	1	5	7M
HYPERPLASIA - NODULAR, ACINI, FOCAL OR MULTIFOCAL:	0	0	0	1	4	5
	0.01	0	0	0	6	6
	0.1	0	0	0	6	6
	0.5	0	0	0	3	3
	2.0	0	0	0	7	7

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
BONE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	12	43	58
	0.01	7	3	3	47	60
	0.1	1	1	10	46	58
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
OSTEOGENIC SARCOMA, (FEMUR), MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
OSTEOGENIC SARCOMA, VARIOUS SITES, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
FIBROSIS, CERVICAL VERTEBRAE, FOCAL:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CARTILAGINOUS EXOSTOSIS, (RIB), FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
BONE MARROW						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	0	2	13	44	59
	0.01	6	3	3	47	59
	0.1	2	1	10	46	59
	0.5	2	5	9	44	60
	2.0	3	2	18	34	57

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
BONE MARROW (CONTINUED)						
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
HYPERPLASIA, MYELOID:	0	1	0	0	0	1
	0.01	1	0	0	0	1
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	1	0	1	0	2
ADRENAL						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	6	3	3	47	59
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	7	16	26
	0.01	3	0	3	13	19
	0.1	2	1	4	19	26
	0.5	2	2	6	16	26
	2.0	3	0	4	15	22
PHEOCHROMOCYTOMA, BENIGN, PRIMARY:	0	0	0	0	3	3
	0.01	0	1	0	6	7
	0.1	0	0	2	5	7
	0.5	0	0	1	4	5
	2.0	0	0	3	7	10*M
PHEOCHROMOCYTOMA, BENIGN, PRIMARY, (TWO):	0	0	0	0	0	0[c]
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0*M
PHEOCHROMOCYTOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	2	2
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
PHEOCHROMOCYTOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0.05.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.

[c] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH THE DATA FROM RATS HAVING ONLY ONE ADENOMA. ANY INDICATED SIGNIFICANCE IN THIS DIAGNOSTIC CATEGORY IS FOR THE COMBINED VALUES.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS	0	1	2	13	44	60
NECROPSIED DURING	0.01	7	3	3	47	60
THE TIME PERIOD	0.1	2	1	11	46	60
INDICATED	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
ADRENAL (CONTINUED)						
GANGLIONEUROMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
DILATED, SINUSOIDS, FOCAL OR MULTIFOCAL:	0	0	0	1	3	4
	0.01	0	0	0	2	2
	0.1	0	0	0	1	1
	0.5	0	0	0	3	3
	2.0	0	0	0	2	2
FIBROSIS, CAPSULE, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
FOCUS(I) OF ALTERED CELLS, CORTEX, FOCAL:	0	0	0	3	19	22
	0.01	2	2	0	19	23
	0.1	0	0	1	10	11M
	0.5	0	2	2	11	15
	2.0	0	2	7	6	15
FOCUS(I) OF ALTERED CELLS, CORTEX, MULTIFOCAL:	0	0	0	0	2	2
	0.01	0	0	0	7	7
	0.1	0	0	1	8	9*M
	0.5	0	0	0	6	6
	2.0	1	0	2	4	7M
TOTAL RATS WITH ONE OR MORE FOCI OF ALTERED CELLS, CORTEX:	0	0	0	3	21	24
	0.01	2	2	0	26	30
	0.1	0	0	2	18	20
	0.5	0	2	2	17	21
	2.0	1	2	9	10	22
HYPERPLASIA, MEDULLA, UNILATERAL:	0	0	0	1	4	5
	0.01	1	1	0	6	8
	0.1	0	0	1	5	6
	0.5	0	1	0	7	8
	2.0	0	0	3	4	7
HYPERPLASIA, MEDULLA, BILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	0	0	2	0	2

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0.05.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
ADRENAL (CONTINUED)						
INFLAMMATION - SUPPURATIVE, CORTEX, BILATERAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
NECROSIS, CORTEX, MULTIFOCAL - SLIGHT:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	2	0	2
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
KIDNEY						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	2	0	0	0	2
ADENOMA, TUBULE(S), BENIGN, PRIMARY:	0	0	0	0	2	2
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CARCINOMA, PELVIC EPITHELIUM, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
LIPOSARCOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
MESENCHYMAL TUMOR, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
KIDNEY (CONTINUED)						
PARAFOLLICULAR CELL ADENOCARCINOMA, MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
CAST(S), TUBULE(S), MULTIFOCAL - VERY SLIGHT:	0	0	0	0	0	0
	0.01	2	1	1	0	4M
	0.1	0	0	0	1	1
	0.5	0	2	1	0	3
	2.0	1	0	2	0	3
CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY, BILATERAL - VERY SLIGHT:	0	0	2	12	16	30
	0.01	3	2	2	14	21
	0.1	1	1	6	19	27
	0.5	1	2	5	18	26
	2.0	1	1	7	11	20
CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY, BILATERAL - SLIGHT:	0	1	0	0	19	20
	0.01	1	0	0	25	26
	0.1	0	0	5	13	18
	0.5	1	0	3	19	23
	2.0	0	1	6	20	27
CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY, BILATERAL - MODERATE:	0	0	0	0	9	9
	0.01	0	0	0	6	6
	0.1	1	0	0	11	12
	0.5	0	0	0	7	7
	2.0	0	0	2	3	5
CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY, BILATERAL - SEVERE:	0	0	0	1	0	1[b]
	0.01	0	0	0	2	2
	0.1	0	0	0	2	2
	0.5	0	0	0	0	0
	2.0	0	0	1	1	2
TOTAL RATS WITH CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY - ANY DEGREE:	0	1	2	13	44	60
	0.01	4	2	2	47	55
	0.1	2	1	11	45	59
	0.5	2	2	8	44	56
	2.0	1	2	16	35	54
CYST, CORTEX, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), $\alpha=0.05$.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
KIDNEY (CONTINUED)						
DEGENERATION - VACUOLAR, TUBULE(S), BILATERAL, DIFFUSE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
INFARCT, FOCAL OR MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	1	0	0	1
	2.0	0	0	0	0	0
MINERALIZATION, PELVIC EPITHELIUM OR TUBULES, MULTIFOCAL - SLIGHT OR MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	1	2
	2.0	0	0	0	0	0
PIGMENT - HEMATOGENOUS - INCREASED, TUBULE(S):	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
THROMBUS - CHRONIC OR ORGANIZED, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
HYDRONEPHROSIS, BILATERAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	0	1
	2.0	0	0	0	0	0
STOMACH						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	6	42	51
	0.01	2	3	2	44	51
	0.1	2	0	5	45	52
	0.5	0	2	3	42	47
	2.0	4	2	10	31	47

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
STOMACH (CONTINUED)						
SQUAMOUS PAPILLOMA, NONGLANDULAR MUCOSA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
LEIOMYOSARCOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
EDEMA, GLANDULAR SUBMUCOSA, DIFFUSE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	0	1
	2.0	0	0	0	0	0
EDEMA, NONGLANDULAR SUBMUCOSA:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	0	0	1
	2.0	0	0	2	0	2
EROSION, GLANDULAR MUCOSA, FOCAL OR MULTIFOCAL:	0	0	0	3	0	-3
	0.01	1	0	0	1	2
	0.1	0	0	1	1	2
	0.5	0	1	1	0	2
	2.0	0	0	3	0	3
HYPERPLASIA - EPITHELIAL, NONGLANDULAR MUCOSA, FOCAL:	0	0	0	0	2	2
	0.01	0	0	1	1	2
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
HYPERPLASIA - EPITHELIAL, NONGLANDULAR MUCOSA, DIFFUSE:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC ACTIVE, NONGLANDULAR SUBMUCOSA, MULTIFOCAL OR DIFFUSE - MODERATE:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	0	1	0	0	1
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
STOMACH (CONTINUED)						
ULCER, GLANDULAR MUCOSA, FOCAL OR MULTIFOCAL:	0	0	0	1	0	1
	0.01	3	0	0	0	3
	0.1	0	0	1	0	1
	0.5	0	0	2	1	3
	2.0	0	0	3	0	3
ULCER, NONGLANDULAR MUCOSA, FOCAL OR MULTIFOCAL:	0	0	0	2	0	2
	0.01	2	0	0	1	3
	0.1	0	0	5	0	5
	0.5	1	1	3	0	5
	2.0	0	0	4	0	4
HYDROPIC DEGENERATION, NONGLANDULAR MUCOSA, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
SMALL INTESTINE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	12	44	59
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	18	32	56
LEIOMYOMA, BENIGN, PRIMARY:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
FIBRIN, LUMEN:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
INFLAMMATION - SUPPURATIVE, TRANSMURAL, FOCAL - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SMALL INTESTINE (CONTINUED)						
INFLAMMATION - SUBACUTE TO CHRONIC, SEROSA, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	2	2
CECUM						
NUMBER OF TISSUES EXAMINED	0	1	2	12	44	59
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	11	44	58
	0.01	7	3	3	47	60
	0.1	2	1	11	45	59
	0.5	2	4	8	44	58
	2.0	3	2	19	35	59
HEMANGIOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
STROMAL POLYP, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
EDEMA, SUBMUCOSA, DIFFUSE:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	0	1
	2.0	0	0	0	0	0
INFLAMMATION - SUBACUTE, SUBMUCOSA - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
LARGE INTESTINE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
LARGE INTESTINE (CONTINUED)						
WITHIN NORMAL LIMITS:	0	1	1	9	34	45
	0.01	6	3	3	39	51
	0.1	2	1	8	33	44
	0.5	2	4	9	37	52
	2.0	4	2	14	24	44
NEUROFIBROMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
POLYPOID ADENOMA, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
EDEMA, SUBMUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	1	0	0	1
	2.0	0	0	0	0	0
PARASITES - NEMATODE, LUMEN:	0	0	1	4	9	14
	0.01	1	0	0	8	9
	0.1	0	0	1	12	13
	0.5	0	0	0	7	7
	2.0	0	0	5	10	15
CERVICAL LYMPH NODE						
NUMBER OF TISSUES EXAMINED	0	1	2	1	7	11
	0.01	0	2	1	8	11
	0.1	2	0	1	9	12
	0.5	1	2	2	6	11
	2.0	1	0	4	7	12
WITHIN NORMAL LIMITS:	0	1	2	1	7	11
	0.01	0	2	1	8	11
	0.1	2	0	1	9	12
	0.5	1	2	2	6	11
	2.0	1	0	4	7	12
MEDIASTINAL LYMPH NODE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	2	3	46	58
	0.1	2	0	11	44	57
	0.5	2	5	9	41	57
	2.0	4	2	19	34	59

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
MEDIASTINAL LYMPH NODE (CONTINUED)						
WITHIN NORMAL LIMITS:	0	0	2	11	44	57
	0.01	7	2	3	46	58
	0.1	2	0	11	44	57
	0.5	2	5	9	40	56
	2.0	4	2	17	33	56
CARCINOMA, (LUNG), MALIGNANT, SECONDARY:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEPLETION OF LYMPHOID ELEMENTS:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC ACTIVE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
INFLAMMATION - SUPPURATIVE - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
PLASMACYTOSIS OF MEDULLARY CORDS:	0	1	0	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
SINUS HISTIOCYTOSIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
MESENTERIC LYMPH NODE						
NUMBER OF TISSUES EXAMINED	0	1	1	11	44	57
	0.01	6	3	3	47	59
	0.1	2	1	11	45	59
	0.5	2	5	8	43	58
	2.0	4	2	19	35	60

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
MESENTERIC LYMPH NODE (CONTINUED)						
WITHIN NORMAL LIMITS:	0	1	1	10	43	55
	0.01	6	3	3	46	58
	0.1	2	1	11	43	57
	0.5	2	5	7	43	57
	2.0	2	2	17	34	55
LEIOMYOSARCOMA, (STOMACH), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
CYSTIC DILATATION, SINUSOIDS:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
DEPLETION OF LYMPHOID ELEMENTS:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
PIGMENT - GOLDEN BROWN (HEMATOGENOUS):	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
PLASMACYTOSIS OF MEDULLARY CORDS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
SINUS HISTIOCYTOSIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	1	0	2	0	3
OTHER MISCELLANEOUS LYMPH NODES						
NUMBER OF TISSUES EXAMINED	0	0	0	1	1	2
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	1	0	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
OTHER MISCELLANEOUS LYMPH NODES (CONTINUED)						
ADENOCARCINOMA, (ISLETS), PANCREATIC, MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CYSTIC DILATATION, SINUSOIDS-RENAL NODE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	0	0	1
HYPERPLASIA - REACTIVE, LYMPHOID, PANCREATIC:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
PLASMACYTOSIS OF MEDULLARY CORDS, VARIOUS NODES:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
SINUS HISTIOCYTOSIS, PANCREATIC:	0	0	0	0	1	-1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
TESTICLE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	0	0	0	1
	0.01	2	0	0	0	2
	0.1	0	0	0	0	0
	0.5	1	0	0	0	1
	2.0	2	0	1	0	3
LEYDIG CELL TUMOR, BENIGN, PRIMARY:	0	0	1	12	44	57
	0.01	5	3	3	46	57
	0.1	2	1	10	44	57
	0.5	0	5	8	42	55
	2.0	2	2	18	35	57

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
TESTICLE (CONTINUED)						
LEYDIG CELL TUMOR, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
MESOTHELIOMA, TUNIC, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	2	2
	0.01	0	0	0	0	0
	0.1	0	0	2	3	5
	0.5	0	0	0	8	8*M
	2.0	0	0	1	6	7M
MESOTHELIOMA, TUNIC, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	3	0	3
	2.0	0	0	1	2	3
TOTAL RATS WITH MESOTHELIOMA, MALIGNANT, WITH OR WITHOUT METASTASIS (EXTENSION TO ORGANS OF THE ABDOMINAL CAVITY)	0	0	0	1	2	3
	0.01	0	0	0	0	0
	0.1	0	0	2	5	7
	0.5	0	0	3	8	11*M
	2.0	0	0	2	8	10*M
REACTIVE MESOTHELIUM WITH OR WITHOUT CHRONIC INFLAMMATION, EPIDIDYMAL LIGAMENT OR MESOEPIDIDYMIS - SLIGHT:	0	0	1	0	3	4
	0.01	0	0	0	8	8
	0.1	0	0	0	3	3
	0.5	1	0	0	3	4
	2.0	0	0	1	4	5
ATROPHY, UNILATERAL, DIFFUSE:	0	0	0	1	5	6
	0.01	0	0	0	2	2
	0.1	1	0	0	2	3
	0.5	0	0	0	3	3
	2.0	0	0	1	4	5
ATROPHY, BILATERAL, DIFFUSE:	0	0	1	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DECREASED SPERMATOGENESIS, BILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	0	0	1
	2.0	0	0	0	0	0
HYPERPLASIA, INTERSTITIAL CELL(S), MULTIFOCAL:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	1	1	2
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0.05.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
TESTICLE (CONTINUED)						
PERIARTERITIS, UNILATERAL - SLIGHT OR MODERATE:	0	0	0	1	1	2
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
PERIARTERITIS, BILATERAL - MODERATE OR SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
EPIDIDYMIS						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	1	13	35	50
	0.01	7	3	3	37	50
	0.1	1	1	10	35	47
	0.5	2	4	8	31	45
	2.0	3	2	16	29	50
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, MULTIFOCAL - SLIGHT:	0	0	1	0	9	10
	0.01	0	0	0	10	10
	0.1	0	0	1	10	11
	0.5	0	0	0	11	11
	2.0	1	0	2	5	8
FIBROSIS, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
GRANULOMA(S) - MICRO, INTERSTITIUM, MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
SPERM GRANULOMA, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	1	0	0	1	2
	0.5	0	1	0	1	2
	2.0	0	0	1	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SEMINAL VESICLE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	0	2	12	44	58
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
INFLAMMATION - NECROTIZING OR SUPPURATIVE - MODERATE:	0	1	0	1	0	2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
COAGULATING GLAND						
NUMBER OF TISSUES EXAMINED	0	1	2	12	44	59
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	34	59
WITHIN NORMAL LIMITS:	0	0	2	11	44	57
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	1	19	34	58
INFLAMMATION - NECROTIZING, BILATERAL - SEVERE:	0	1	0	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE OR SUBACUTE TO CHRONIC - SLIGHT:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	0	0	1
PROSTATE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
PROSTATE (CONTINUED)						
WITHIN NORMAL LIMITS:	0	0	2	6	28	36
	0.01	7	2	1	21	31
	0.1	2	1	10	23	36
	0.5	2	4	5	23	34
	2.0	4	1	13	21	39
ADENOCARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	0	1
	2.0	0	0	0	0	0
ABSCESS - SEVERE:	0	0	0	2	0	2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CYST, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION WITH OR WITHOUT INFLAMMATION, GLANDS - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	2	2
	0.1	0	0	0	2	2
	0.5	0	0	0	2	2
	2.0	0	0	0	1	1
HYPERPLASIA - ADENOMATOUS, MUCOSA, FOCAL OR MULTIFOCAL:	0	0	0	1	8	9
	0.01	0	0	1	10	11
	0.1	0	0	0	12	12
	0.5	0	0	1	13	14
	2.0	0	0	2	10	12
INFLAMMATION - NECROTIZING - SEVERE:	0	1	0	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUBACUTE TO CHRONIC, FOCAL OR MULTIFOCAL:	0	0	0	4	10	14
	0.01	0	1	1	17	19
	0.1	0	0	1	13	14
	0.5	0	0	4	8	12
	2.0	0	1	6	4	11
URINARY BLADDER						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	6	3	3	47	59
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
URINARY BLADDER (CONTINUED)						
WITHIN NORMAL LIMITS:	0	1	2	11	44	58
	0.01	6	3	3	47	59
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	33	58
EDEMA, SUBMUCOSA, FOCAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
HYPERPLASIA, MUCOSA, DIFFUSE - MODERATE:	0	0	0	2	0	2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
URETHRA						
NUMBER OF TISSUES EXAMINED	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
METAPLASIA - SQUAMOUS, MUCOSA, FOCAL:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
LUNGS						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	2	3	47	59
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	0	8	16	25
	0.01	7	2	3	20	32
	0.1	2	1	7	20	30
	0.5	2	4	6	15	27
	2.0	2	0	10	15	27
ADENOMA, ALVEOLI, BENIGN, PRIMARY:	0	0	0	0	5	5
	0.01	0	0	0	1	1
	0.1	0	0	0	3	3
	0.5	0	0	0	2	2
	2.0	0	0	0	3	3

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
LUNGS (CONTINUED)						
ADENOMA, BRONCHIOLES, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CARCINOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	1	1	0	2
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
CARCINOMA, (AUDITORY SEBACEOUS GLAND), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	2	0	2
PHEOCHROMOCYTOMA, MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
FIBROSARCOMA, (SKIN), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
ALVEOLAR HISTIOCYTOSIS, FOCAL OR MULTIFOCAL - SLIGHT:	0	0	0	1	7	8
	0.01	0	0	0	8	8
	0.1	0	0	1	7	8
	0.5	0	1	0	8	9
	2.0	0	0	4	7	11
ALVEOLAR HISTIOCYTOSIS, MULTIFOCAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
ATELECTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
CHRONIC PASSIVE CONGESTIVE CHANGES:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	2	0	1	0	3

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS	0	1	2	13	44	60
NECROPSIED DURING	0.01	7	3	3	47	60
THE TIME PERIOD	0.1	2	1	11	46	60
INDICATED	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
LUNGS (CONTINUED)						
HYPERPLASIA - ADENOMATOUS, ALVEOLI, FOCAL OR MULTIFOCAL:	0	0	0	0	7	7
	0.01	0	0	0	1	1M
	0.1	0	0	0	3	3
	0.5	0	0	0	6	6
	2.0	0	0	0	2	2
INFLAMMATION - ACUTE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, INTERSTITIUM, MULTIFOCAL - SLIGHT OR MODERATE:	0	0	0	0	14	14
	0.01	0	0	0	19	19
	0.1	0	0	1	13	14
	0.5	0	0	0	14	14
	2.0	0	2	2	12	16
INFLAMMATION - SUBACUTE, FOCAL OR MULTIFOCAL - SLIGHT:	0	0	1	0	1	2
	0.01	0	0	0	4	4
	0.1	0	0	0	1	1
	0.5	0	0	0	6	6
	2.0	0	0	0	1	1
INFLAMMATION - SUBACUTE OR SUPPURATIVE, MULTIFOCAL - MODERATE:	0	0	0	1	0	-1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	3	0	3
NECROSIS, MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
INFLAMMATION - SUBACUTE TO CHRONIC, INTERSTITIUM, FOCAL OR MULTIFOCAL:	0	0	0	1	3	4
	0.01	0	0	0	2	2
	0.1	0	0	0	3	3
	0.5	0	0	0	5	5
	2.0	0	0	0	4	4
SKELETAL MUSCLE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	13	44	60
	0.01	5	3	3	47	58
	0.1	1	1	9	46	57
	0.5	2	4	9	44	59
	2.0	4	2	18	34	58

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SKELETAL MUSCLE (CONTINUED)						
DEGENERATION WITH OR WITHOUT INFLAMMATION, MUSCLE FIBERS - VERY SLIGHT OR SLIGHT:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	1	0	2	0	3
	0.5	0	1	0	0	1
	2.0	0	0	1	1	2
DEGENERATION WITH OR WITHOUT INFLAMMATION, MUSCLE FIBERS - MODERATE:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SALIVARY GLAND						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	6	3	3	47	59
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	18	35	59
WITHIN NORMAL LIMITS:	0	1	2	13	41	57
	0.01	6	3	3	43	55
	0.1	1	1	11	45	58
	0.5	2	5	9	44	60
	2.0	4	2	18	31	55
UNDIFFERENTIATED SARCOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ATROPHY, ACINI, FOCAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ATROPHY, ACINI, UNILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DILATATION, DUCTS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SALIVARY GLAND (CONTINUED)						
FIBROSIS, INTERSTITIUM, UNILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	2	2
INFLAMMATION - CHRONIC, FOCAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
THYMUS						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	6	2	3	45	56
	0.1	2	0	10	42	54
	0.5	2	5	9	43	59
	2.0	4	2	19	33	58
WITHIN NORMAL LIMITS:	0	1	2	13	43	59
	0.01	6	2	3	44	55
	0.1	2	0	10	39	51
	0.5	2	5	9	40	56
	2.0	4	2	17	32	55
CYST:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	3	3
	0.5	0	0	0	3	3
	2.0	0	0	2	1	3
MEDIASTINAL TISSUE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	2	3	47	59
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	11	43	57
	0.01	7	2	3	44	56
	0.1	2	1	10	42	55
	0.5	2	5	8	41	56
	2.0	4	2	19	34	59

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS	0	1	2	13	44	60
NECROPSIED DURING	0.01	7	3	3	47	60
THE TIME PERIOD	0.1	2	1	11	46	60
INDICATED	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
MEDIASTINAL TISSUE (CONTINUED)						
MESOTHELIOMA, PLEURA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CARCINOMA, (LUNG), MALIGNANT, SECONDARY:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	3	3
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
INFLAMMATION - CHRONIC, MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
ECTOPIC PARATHYROID:	0	0	0	1	0	1
	0.01	0	0	0	2	2
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
AORTA						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	2	3	47	59
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	13	44	60
	0.01	7	2	3	47	59
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
ESOPHAGUS						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	2	3	47	59
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS	0	1	2	13	44	60
NECROPSIED DURING	0.01	7	3	3	47	60
THE TIME PERIOD	0.1	2	1	11	46	60
INDICATED	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
ESOPHAGUS (CONTINUED)						
WITHIN NORMAL LIMITS:	0	1	2	12	44	59
	0.01	7	2	3	47	59
	0.1	2	0	11	46	59
	0.5	2	5	9	44	60
	2.0	4	2	18	35	59
SQUAMOUS CELL CARCINOMA, (PHARYNX), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
HYPERKERATOSIS:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	1	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
THYROID GLAND						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	6	2	3	47	58
	0.1	2	1	11	45	59
	0.5	2	5	9	43	59
	2.0	4	2	19	34	59
WITHIN NORMAL LIMITS:	0	1	2	8	17	28
	0.01	4	2	3	25	34
	0.1	2	1	6	23	32
	0.5	2	5	9	26	42
	2.0	2	2	9	17	30
ADENOMA, FOLLICLE(S), BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	1	1	2
	0.5	0	0	0	1	1
	2.0	0	0	2	5	7*M
PARAFOLLICULAR CELL ADENOCARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	1	1
	2.0	0	0	2	0	2
PARAFOLLICULAR CELL ADENOCARCINOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
PARAFOLLICULAR CELL ADENOMA, BENIGN, PRIMARY:	0	0	0	2	6	8
	0.01	0	0	0	9	9
	0.1	0	0	1	8	9
	0.5	0	0	0	5	5
	2.0	0	0	2	4	6

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0.05.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS	0	1	2	13	44	60
NECROPSIED DURING	0.01	7	3	3	47	60
THE TIME PERIOD	0.1	2	1	11	46	60
INDICATED	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
THYROID GLAND (CONTINUED)						
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CYSTIC DILATATION, FOLLICLE(S), FOCAL:	0	0	0	1	2	3
	0.01	0	0	0	2	2
	0.1	0	0	0	4	4
	0.5	0	0	0	1	1
	2.0	0	0	3	4	7
DEGENERATION, FOLLICLE(S), FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	0	0	0	0
HYPERPLASIA, PARAFOLLICULAR CELLS, FOCAL OR MULTIFOCAL:	0	0	0	1	18	19
	0.01	1	0	0	10	11
	0.1	0	0	2	10	12
	0.5	0	0	0	8	8M
	2.0	1	0	3	4	8
CYST(S) WITH KERATINOUS DEBRIS, FOCAL:	0	0	0	0	1	1
	0.01	1	0	0	2	3
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	1	0	0	1	2
PARATHYROID GLAND						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	6	3	3	46	58
	0.1	1	1	10	44	56
	0.5	2	4	9	42	57
	2.0	4	2	19	34	59
WITHIN NORMAL LIMITS:	0	1	2	12	42	57
	0.01	6	3	2	43	54
	0.1	1	1	9	40	51
	0.5	2	4	8	39	53
	2.0	4	2	18	32	56
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO', $p \leq 0.05$.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
PARATHYROID GLAND (CONTINUED)						
DILATED, SINUSOIDS, UNILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
HYPERPLASIA, UNILATERAL, FOCAL:	0	0	0	1	2	3
	0.01	0	0	1	3	4
	0.1	0	0	1	4	5
	0.5	0	0	1	2	3
	2.0	0	0	0	1	1
HYPERPLASIA - SECONDARY TO KIDNEY DISEASE, BILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
TRACHEA						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SKIN						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	8	44	59
	2.0	4	2	18	35	59
WITHIN NORMAL LIMITS:	0	1	2	11	42	56
	0.01	7	3	2	43	55
	0.1	2	1	9	37	49
	0.5	2	4	8	35	49
	2.0	4	1	16	31	52
ADENOMA, SEBACEOUS GLANDS, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	1	2

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SKIN (CONTINUED)						
BASAL CELL ADENOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	0	0	1	0	1
CARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
KERATOACANTHOMA, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
SQUAMOUS PAPILLOMA, VARIOUS LOCATIONS, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
FIBROMA, VARIOUS LOCATIONS, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	2	3
	0.5	0	0	0	2	2
	2.0	0	0	0	0	0
FIBROSARCOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	0	0	0	0
FIBROSARCOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
HEMANGIOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
LIPOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	3	3
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
SKIN (CONTINUED)						
MYXOMA, EAR, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
UNDIFFERENTIATED SARCOMA, SUBCUTANEOUS, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
ABSCESS, VARIOUS LOCATIONS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
EPIDERMAL INCLUSION CYST:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	0	1
	2.0	0	0	0	1	1
HYPERPLASIA - EPITHELIAL, EXTERNAL NARES, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
INFARCT, TAIL:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC ACTIVE, SUBCUTANEOUS, FOCAL - SLIGHT OR MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CELLULITIS, (REAR FOOT) - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	0	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
MAMMARY GLAND						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	1	5	8	44	58
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	1	9	20	31
	0.01	5	1	2	22	30
	0.1	2	0	2	23	27
	0.5	0	3	2	25	30
	2.0	3	0	8	16	27
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
FIBROADENOMA, BENIGN, PRIMARY:	0	0	0	1	2	3
	0.01	0	0	0	2	2
	0.1	0	0	2	2	4
	0.5	0	0	0	2	2
	2.0	0	0	0	3	3
FIBROMA, BENIGN, PRIMARY:	0	0	0	0	3	-3
	0.01	0	0	1	3	4
	0.1	0	0	2	3	5
	0.5	0	0	1	2	3
	2.0	0	0	3	3	6
FIBROMA, BENIGN, PRIMARY, (TWO):	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
FIBROMA, BENIGN, PRIMARY, (THREE):	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
TOTAL RATS WITH ONE OR MORE BENIGN MAMMARY TUMORS:	0	0	0	1	6	7
	0.01	0	0	1	5	6
	0.1	0	0	3	5	8
	0.5	0	0	2	4	6
	2.0	0	0	4	6	10

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
MAMMARY GLAND (CONTINUED)						
DILATATION, DUCTS:	0	0	1	3	16	20
	0.01	1	2	0	15	18
	0.1	0	0	7	13	20
	0.5	1	2	4	16	23
	2.0	1	0	7	7	15
GALACTOCELE:	0	0	0	0	3	3
	0.01	0	0	0	1	1
	0.1	0	0	0	3	3
	0.5	0	0	0	1	1
	2.0	0	0	0	3	3
GALACTOCELE, (TWO):	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
PIGMENT-LADEN MACROPHAGES, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
HYPERPLASIA OFTEN ACCOMPANIED BY DUCT ECTASIA:	0	0	0	1	3	-4
	0.01	1	0	1	6	8
	0.1	0	1	0	3	4
	0.5	0	0	0	2	2
	2.0	0	2	1	5	8
PREPUTIAL GLAND						
NUMBER OF TISSUES EXAMINED	0	1	0	0	3	4
	0.01	0	0	0	5	5
	0.1	0	0	0	2	2
	0.5	0	0	0	2	2
	2.0	0	0	2	2	4
WITHIN NORMAL LIMITS:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
PREPUTIAL GLAND (CONTINUED)						
IMPACTION WITH OR WITHOUT CELLULAR DEBRIS OR WITH OR WITHOUT INFLAMMATION, UNILATERAL:	0	0	0	0	1	1
	0.01	0	0	0	3	3
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
INFLAMMATION - CHRONIC ACTIVE OR NECROTIZING, UNILATERAL - SEVERE:	0	1	0	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	1	0	1
EYE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	12	41	56
	0.01	6	3	3	42	54
	0.1	2	1	9	42	54
	0.5	2	4	9	42	57
	2.0	4	2	15	32	53
CATARACT, LENS, UNILATERAL OR BILATERAL:	0	0	0	0	1	1
	0.01	0	0	0	3	3
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	0	0	2	2
DEGENERATION, RETINA, UNILATERAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
DEGENERATION, RETINA, BILATERAL - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
INCREASED VASCULARITY, CORNEA, UNILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
EYE (CONTINUED)						
INFLAMMATION - CHRONIC ACTIVE, CORNEA, UNILATERAL - MODERATE OR SEVERE:	0	0	0	1	1	2
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
INFLAMMATION - SUPPURATIVE, ANTERIOR CHAMBER, UNILATERAL - SLIGHT OR MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	1	0	0	1
	2.0	0	0	1	0	1
PHTHISIS BULBI, UNILATERAL:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	3	3
	0.5	0	0	0	0	0
	2.0	0	0	1	1	2
TONGUE						
NUMBER OF TISSUES EXAMINED	0	1	2	12	44	59
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	1	12	31	45
	0.01	7	2	3	32	44
	0.1	1	1	11	42	55
	0.5	2	5	9	36	52
	2.0	4	2	17	26	49
SQUAMOUS CELL CARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SQUAMOUS PAPILLOMA, BENIGN, PRIMARY:	0	0	0	0	2	2
	0.01	0	0	0	3	3
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, SUBMUCOSA - SLIGHT:	0	0	0	0	9	9
	0.01	0	0	0	5	5
	0.1	0	0	0	2	2M
	0.5	0	0	0	4	4
	2.0	0	0	0	5	5

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
TONGUE (CONTINUED)						
CYSTIC DILATATION, SALIVARY GLAND DUCT:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
HYPERPLASIA - EPITHELIAL, FOCAL:	0	0	0	0	0	0
	0.01	0	1	0	2	3
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	3	3
INFLAMMATION - CHRONIC, PERINEURAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
PERIARTERITIS - SLIGHT OR MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	4	4
	0.1	1	0	0	2	3
	0.5	0	0	0	2	2
	2.0	0	0	1	1	2
FOREIGN BODY REACTION (USUALLY ASSOCIATED WITH SUBMUCOSAL GLANDS) FOCAL:	0	0	1	0	2	3
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	0	1	0	1
ORAL TISSUES						
NUMBER OF TISSUES EXAMINED	0	1	0	5	7	13
	0.01	0	0	2	10	12
	0.1	1	1	0	7	9
	0.5	1	1	1	13	16
	2.0	0	0	1	11	12
SQUAMOUS CELL CARCINOMA, VARIOUS LOCATIONS, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	1	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	1	1	2
SQUAMOUS PAPILLOMA, HARD PALATE OR LIP, BENIGN, PRIMARY:	0	0	0	0	2	2
	0.01	0	0	1	3	4
	0.1	0	0	0	0	0
	0.5	0	0	0	4	4
	2.0	0	0	0	4	4

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
ORAL TISSUES (CONTINUED)						
ABSCESS, LIP, FOCAL:	0	1	0	0	0	1
	0.01	0	0	0	0	0
	0.1	1	0	0	1	2
	0.5	0	1	0	0	1
	2.0	0	0	0	0	0
HYPERPLASIA - EPITHELIAL, HARD PALATE, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	1	3	4M
	2.0	0	0	0	5	5*M
INFLAMMATION - CHRONIC ACTIVE, PERIDONTAL, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	2	2
	2.0	0	0	0	3	3
ULCER, LIP, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	0	0	1
	2.0	0	0	0	0	0
CYST(S) WITH KERATINOUS DEBRIS, PERIDONTAL, FOCAL:	0	0	0	3	1	4
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0M
FOREIGN BODY REACTION, PERIDONTAL, FOCAL OR MULTIFOCAL:	0	0	0	2	4	6
	0.01	0	0	1	6	7
	0.1	0	0	0	3	3
	0.5	0	0	0	5	5
	2.0	0	0	0	2	2
NASAL TISSUES						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	2	8	25	36
	0.01	5	1	3	34	43
	0.1	1	0	3	34	38
	0.5	1	4	5	30	40
	2.0	4	1	12	20	37

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0.05.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURES (PETO), α=0.05.
T INDICATES A LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, α=0.05.
t INDICATES A LINEAR TREND BY MANTEL-HAENSZEL EXTENSION OF THE COCHRAN-ARMITAGE TEST (PETO), α=0.05.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
NASAL TISSUES (CONTINUED)						
ADENOMA, SUBMUCOSAL GLANDS, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
SQUAMOUS PAPILLOMA, NASOLACRIMAL DUCT, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
UNDIFFERENTIATED CARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION, OLFACTORY EPITHELIUM, FOCAL OR MULTIFOCAL - SLIGHT OR MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	1	0	0	1	2
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC ACTIVE OR SUPPURATIVE, OLFACTORY EPITHELIUM - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC ACTIVE OR SUPPURATIVE, RESPIRATORY EPITHELIUM - SLIGHT OR MODERATE:	0	0	0	0	6	6
	0.01	0	0	0	3	3
	0.1	0	0	0	3	3
	0.5	1	0	1	3	5
	2.0	0	0	1	4	5
INFLAMMATION - CHRONIC ACTIVE OR SUPPURATIVE, NASOLACRIMAL DUCT, UNILATERAL:	0	0	0	0	0	0
	0.01	0	1	0	1	2
	0.1	0	0	3	0	3
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
THROMBUS - ACUTE OR RECENT, MULTIFOCAL:	0	0	0	3	0	3
	0.01	0	0	0	0	0
	0.1	1	0	2	0	3
	0.5	0	0	4	0	4
	2.0	0	0	3	0	3

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
NASAL TISSUES (CONTINUED)						
CYST(S) WITH KERATINOUS DEBRIS, NASOLACRIMAL DUCT, UNILATERAL:	0	0	0	0	6	6
	0.01	1	1	0	3	5
	0.1	1	0	1	4	6
	0.5	0	0	0	4	4
	2.0	0	0	1	5	6
FOREIGN BODY REACTION, FOCAL OR MULTIFOCAL:	0	0	0	2	8	10
	0.01	1	0	0	4	5
	0.1	0	1	3	5	9
	0.5	0	1	0	5	6
	2.0	0	1	2	8	11
FOREIGN BODY REACTION, NASOLACRIMAL DUCT, UNILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
MESENTERIC TISSUE						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	1	8	29	39
	0.01	6	3	3	37	49
	0.1	1	0	6	35	42
	0.5	1	4	6	33	44
	2.0	4	1	11	27	43
LIPOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ADHESIONS - FIBROUS, MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
ATROPHY, ADIPOSE TISSUE:	0	0	0	5	1	6
	0.01	0	0	0	2	2
	0.1	1	0	5	3	9
	0.5	1	1	3	1	6
	2.0	0	0	6	1	7

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
MESENTERIC TISSUE (CONTINUED)						
ECTOPIC SPLEEN:	0	0	0	1	3	4
	0.01	0	0	0	4	4
	0.1	0	0	0	3	3
	0.5	0	0	0	4	4
	2.0	0	0	0	1	1
FIBROSIS, MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	1	0	2
INFLAMMATION - CHRONIC ACTIVE, FOCAL OR MULTIFOCAL - SLIGHT OR MODERATE:	0	0	0	1	1	2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	1	0	1
STRANGULATED OR NECROTIC FAT:	0	0	1	1	6	8Tt
	0.01	1	0	0	5	6
	0.1	1	1	0	4	6
	0.5	0	0	0	3	3
	2.0	0	0	0	3	3
PERIARTERITIS - SLIGHT OR MODERATE:	0	0	0	1	3	4
	0.01	0	0	0	2	2
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
PERIARTERITIS - SEVERE:	0	0	0	0	3	3[b]Tt
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
LACRIMAL/HARDERIAN GLAND(S)						
NUMBER OF TISSUES EXAMINED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	0	2	8	24	34
	0.01	5	3	3	27	38
	0.1	2	1	9	25	37
	0.5	1	4	7	29	41
	2.0	3	2	14	24	43

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

\- INDICATES A LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, $\alpha=0.05$.

t INDICATES A LINEAR TREND BY MANTEL-HAENSZEL EXTENSION OF THE COCHRAN-ARMITAGE TEST (PETO), $\alpha=0.05$.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
LACRIMAL/HARDERIAN GLAND(S) (CONTINUED)						
UNDIFFERENTIATED CARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, UNILATERAL:	0	1	0	4	11	16
	0.01	1	0	0	12	13
	0.1	0	0	2	16	18
	0.5	0	1	1	9	11
	2.0	1	0	4	5	10
INFLAMMATION - CHRONIC, BILATERAL:	0	0	0	1	4	5
	0.01	0	0	0	3	3
	0.1	0	0	0	2	2
	0.5	1	0	1	3	5
	2.0	0	0	1	3	4
CYST(S) WITH KERATINOUS DEBRIS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION--SECONDARY TO ORBITAL BLEEDING, UNILATERAL:	0	0	0	0	5	5
	0.01	0	0	0	4	4
	0.1	0	0	0	5	5
	0.5	0	0	0	4	4
	2.0	0	0	0	6	6
LARYNX						
NUMBER OF TISSUES EXAMINED	0	1	2	11	44	58
	0.01	6	3	3	46	58
	0.1	2	1	11	45	59
	0.5	2	5	8	44	59
	2.0	4	2	19	35	60
WITHIN NORMAL LIMITS:	0	1	1	10	40	52
	0.01	5	3	3	42	53
	0.1	2	1	10	43	56
	0.5	1	5	8	41	55
	2.0	4	2	15	27	48
PARAFOLLICULAR CELL ADENOCARCINOMA, MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
LARYNX (CONTINUED)						
SQUAMOUS CELL CARCINOMA, (ORAL CAVITY-PHARYNX), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
IMPACTION WITH OR WITHOUT CELLULAR DEBRIS OR WITH OR WITHOUT INFLAMMATION, SUBMUCOSAL GLANDS:	0	0	1	0	4	5
	0.01	1	0	0	4	5
	0.1	0	0	1	1	2
	0.5	1	0	0	3	4
	2.0	0	0	3	7	10
INFLAMMATION - CHRONIC ACTIVE, SUBMUCOSA:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
FOREIGN BODY REACTION, SUBMUCOSA, FOCAL:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
AUDITORY SEBACEOUS (ZYMBAL) GLAND(S)						
NUMBER OF TISSUES EXAMINED	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	2	1	3
	0.5	0	0	0	1	1
	2.0	0	0	3	0	3
WITHIN NORMAL LIMITS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
CARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 23 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Males

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF MALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	1	2	13	44	60
	0.01	7	3	3	47	60
	0.1	2	1	11	46	60
	0.5	2	5	9	44	60
	2.0	4	2	19	35	60
AUDITORY SEBACEOUS (ZYMBAL) GLAND(S) (CONTINUED)						
CARCINOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	2	0	2
MULTIPLE ORGANS						
LEUKEMIA - UNCLASSIFIED, MULTIPLE ORGANS, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	0	1
	2.0	0	0	1	0	1
MESOTHELIOMA, (TESTICLE), MALIGNANT, SECONDARY:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	3	0	3
	2.0	0	0	1	2	3
OSTEOGENIC SARCOMA, VARIOUS SITES, MALIGNANT, SECONDARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
MINERALIZATION--SECONDARY TO RENAL DISEASE, MULTIPLE ORGANS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	1	0	0	1
	2.0	0	0	1	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
PERIPHERAL NERVE, TIBIAL						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	1	1	1	9	12
	0.01	2	1	3	4	10
	0.1	4	0	2	4	10
	0.5	4	0	4	3	11
	2.0	1	4	0	3	8
DEGENERATION - VERY SLIGHT:	0	1	1	5	38	45
	0.01	0	1	4	38	43
	0.1	4	1	2	38	45
	0.5	0	1	8	33	42
	2.0	2	2	16	17	37
DEGENERATION - SLIGHT:	0	0	0	0	3	3
	0.01	0	0	1	6	7
	0.1	0	0	0	5	5
	0.5	0	0	0	7	7
	2.0	1	1	5	6	13
DEGENERATION - MODERATE:	0	0	0	0	0	- 0[b]
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	3	3*M
PERIPHERAL NERVE, SAPHENOUS						
NUMBER OF TISSUES EXAMINED	0	0	0	0	10	10
	0.01	0	0	0	10	10
	0.1	0	0	0	10	10
	0.5	0	0	0	10	10
	2.0	0	0	0	10	10
WITHIN NORMAL LIMITS:	0	-	-	-	9	9
	0.01	-	-	-	9	9
	0.1	-	-	-	8	8
	0.5	-	-	-	10	10
	2.0	-	-	-	10	10

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
- INDICATES NOT APPLICABLE.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, $\alpha=0.05$.

M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), $\alpha=0.05$.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
PERIPHERAL NERVE, SAPHENOUS						
DEGENERATION - VERY SLIGHT:	0	-	-	-	1	1
	0.01	-	-	-	1	1
	0.1	-	-	-	2	2
	0.5	-	-	-	0	0
	2.0	-	-	-	0	0
PERIPHERAL NERVE, BRACHIAL PLEXUS						
NUMBER OF TISSUES EXAMINED	0	0	0	0	10	10
	0.01	0	0	0	9	9
	0.1	0	0	0	10	10
	0.5	0	0	0	10	10
	2.0	0	0	0	10	10
WITHIN NORMAL LIMITS:	0	-	-	-	5	5
	0.01	-	-	-	5	5
	0.1	-	-	-	6	6
	0.5	-	-	-	4	4
	2.0	-	-	-	6	6
DEGENERATION - VERY SLIGHT:	0	-	-	-	5	5
	0.01	-	-	-	3	3
	0.1	-	-	-	4	4
	0.5	-	-	-	6	6
	2.0	-	-	-	3	3
DEGENERATION - SLIGHT:	0	-	-	-	0	0
	0.01	-	-	-	1	1
	0.1	-	-	-	0	0
	0.5	-	-	-	0	0
	2.0	-	-	-	0	0
DEGENERATION - SEVERE:	0	-	-	-	0	0
	0.01	-	-	-	0	0
	0.1	-	-	-	0	0
	0.5	-	-	-	0	0
	2.0	-	-	-	1	1
PERIPHERAL NERVE, TRIGEMINAL						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	6	46	56
	0.01	2	2	8	43	55
	0.1	8	1	4	42	55
	0.5	4	1	11	40	56
	2.0	4	7	21	26	58

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
- INDICATES NOT APPLICABLE.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
PERIPHERAL NERVE, TRIGEMINAL (CONTINUED)						
DEGENERATION - SECONDARY TO ORBITAL BLEEDING, UNILATERAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	3	3
	0.1	0	0	0	2	2
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
DEGENERATION - SECONDARY TO ORBITAL BLEEDING, UNILATERAL - MODERATE:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	3	3
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
DEGENERATION - SECONDARY TO ORBITAL BLEEDING, UNILATERAL - SEVERE:	0	0	0	0	2	2
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	1	3	4
	2.0	0	0	0	1	1
BRAIN						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	1	5	46	54
	0.01	2	1	6	42	51
	0.1	7	1	4	42	54
	0.5	4	1	11	40	56
	2.0	4	3	13	23	43
ASTROCYTOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	1	1	3
OLIGODENDROGLIOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
GRANULAR CELL TUMOR, MENINGES, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	2	2

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
BRAIN (CONTINUED)						
GLIAL PROLIFERATION (SUGGESTIVE OF EARLY TUMOR), FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	2	1	3
ADENOCARCINOMA, (PITUITARY), MALIGNANT, SECONDARY:	0	0	1	0	1	2
	0.01	0	0	1	3	4
	0.1	1	0	0	0	1
	0.5	0	0	1	2	3
	2.0	0	1	1	0	2
UNDIFFERENTIATED CARCINOMA, (NASAL TURBINATES), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
DEGENERATION, OPTIC NERVE, UNILATERAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
GLIOSIS, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	1	0	0	1
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
HEMORRHAGE, MULTIFOCAL - SLIGHT:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
HYDROCEPHALUS, BILATERAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - GRANULOMATOUS, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, MENINGES, DIFFUSE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
BRAIN (CONTINUED)						
VACUOLIZATION, GRAY MATTER, MULTIFOCAL - SEVERE:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
VACUOLIZATION, WHITE MATTER:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
PERIVASCULAR MONONUCLEAR (LYMPHOID) CELL CUFFING, FOCAL OR MULTIFOCAL - VERY SLIGHT OR SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	2	2
	0.1	0	0	0	3	3
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
NECROSIS WITH ACCOMPANYING INFLAMMATION, FOCAL - SLIGHT OR MODERATE:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	0	0	1
SPINAL CORD, CERVICAL REGION						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	47	59
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
ASTROCYTOMA, GRAY MATTER, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	2	2
DEGENERATION, WHITE MATTER - VERY SLIGHT:	0	0	0	0	15	15
	0.01	0	0	3	13	16
	0.1	0	0	1	7	8
	0.5	0	0	4	14	18
	2.0	0	2	2	7	11
DEGENERATION, WHITE MATTER - SLIGHT:	0	0	0	1	0	1
	0.01	0	0	2	1	3
	0.1	0	0	0	3	3
	0.5	0	0	0	0	0
	2.0	0	0	2	0	2

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
SPINAL CORD, CERVICAL REGION (CONTINUED)						
DEGENERATION, WHITE MATTER - MODERATE:	0	0	0	0	0	0[b]
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	1	2
TOTAL RATS WITH DEGENERATION, WHITE MATTER - ANY GRADE:	0	0	0	1	15	16
	0.01	0	0	5	14	19
	0.1	0	0	1	10	11
	0.5	0	0	4	14	18
	2.0	0	2	5	8	15
MALACIA, WHITE MATTER, FOCAL:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, MENINGES, DIFFUSE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
VACUOLIZATION, WHITE MATTER, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SPINAL CORD, THORACIC REGION						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	47	59
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
DEGENERATION, WHITE MATTER - VERY SLIGHT:	0	1	0	1	17	19
	0.01	0	0	2	4	6
	0.1	1	1	1	9	12
	0.5	0	0	3	11	14
	2.0	0	1	6	7	14
DEGENERATION, WHITE MATTER - SLIGHT:	0	0	0	1	2	3
	0.01	0	0	2	2	4
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	4	5	9M
TOTAL RATS WITH DEGENERATION, WHITE MATTER - ANY GRADE:	0	1	0	2	19	22
	0.01	0	0	4	6	10M
	0.1	1	1	1	9	12
	0.5	0	0	3	12	15
	2.0	0	1	10	12	23

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
SPINAL CORD, THORACIC REGION (CONTINUED)						
INFLAMMATION - SUPPURATIVE, MENINGES, DIFFUSE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
VACUOLIZATION, WHITE MATTER, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SPINAL CORD, LUMBOSACRAL REGION						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	47	59
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
ASTROCYTOMA, GRAY MATTER, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
DEGENERATION, WHITE MATTER - VERY SLIGHT:	0	0	0	2	21	23
	0.01	1	1	3	17	22
	0.1	1	0	0	24	25
	0.5	0	0	1	24	25
	2.0	1	1	5	8	15
DEGENERATION, WHITE MATTER - SLIGHT:	0	0	0	0	14	14
	0.01	0	0	1	7	8
	0.1	0	0	0	5	5
	0.5	0	0	0	1	1
	2.0	0	0	2	9	11
DEGENERATION, WHITE MATTER - MODERATE:	0	0	0	0	1	1[b]
	0.01	0	0	0	1	1
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
TOTAL RATS WITH DEGENERATION, WHITE MATTER - ANY GRADE:	0	0	0	2	36	38T
	0.01	1	1	4	25	31
	0.1	1	0	0	31	32
	0.5	0	0	1	26	27
	2.0	1	1	7	17	26

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0.05.

M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), α=0.05.

T LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
SPINAL CORD, LUMBOSACRAL REGION (CONTINUED)						
PERIVASCULAR MONONUCLEAR (LYMPHOID) CELL CUFFING, MENINGES, FOCAL - VERY SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
EPIDERMOID CYST, MENINGES, FOCAL:	0	0	0	0	0	0
	0.01	1	0	0	2	3
	0.1	0	0	0	3	3
	0.5	0	0	0	1	1
	2.0	0	1	0	0	1
LIVER						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	1	1	1	0	3
	0.01	1	1	1	0	3
	0.1	1	0	2	0	3
	0.5	0	0	0	0	0
	2.0	0	1	3	0	4
HYPERPLASTIC (NEOPLASTIC) NODULE, HEPATOCELLULAR, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	2	1	3
	2.0	0	0	0	1	1
UNDIFFERENTIATED CARCINOMA, (NASAL TURBINATES), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ACCENTUATED LOBULAR PATTERN:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, MULTIFOCAL - SLIGHT:	0	0	1	0	30	31
	0.01	1	1	3	27	32
	0.1	4	1	0	29	34
	0.5	0	1	3	17	21
	2.0	1	2	4	12	19
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, MULTIFOCAL - MODERATE:	0	0	0	1	1	2[b]
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1*

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, $\alpha=0.05$.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
LIVER (CONTINUED)						
ARCHITECTURE ALTERED SECONDARY TO DIAPHRAGMATIC HERNIA:	0	0	0	0	2	2
	0.01	0	0	1	2	3
	0.1	1	0	1	2	4
	0.5	0	0	1	6	7M
	2.0	0	1	2	0	3
AREA(S) OF ALTERED CELLS, HEPATOCELLULAR, ONE:	0	0	1	1	21	23
	0.01	0	0	0	10	10
	0.1	0	0	0	18	18
	0.5	0	1	2	11	14
	2.0	0	1	6	7	14
AREA(S) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL, (TWO TO FOUR):	0	0	0	0	9	9
	0.01	0	0	1	11	12
	0.1	0	0	0	12	12
	0.5	0	0	0	16	16
	2.0	0	1	1	9	11
AREA(S) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL - (FIVE OR MORE):	0	0	0	0	1	1[b]t
	0.01	0	0	0	2	2
	0.1	0	0	0	2	2
	0.5	0	0	1	1	2
	2.0	0	0	0	2	2
TOTAL RATS WITH ONE OR MORE AREAS OF ALTERED CELLS:	0	0	1	1	31	33
	0.01	0	0	1	23	24
	0.1	0	0	0	32	32
	0.5	0	1	3	28	32
	2.0	0	2	7	18	27
CYST, BILE DUCTS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION - CYSTIC, HEPATOCELLULAR, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DILATED, SINUSOIDS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
FOCUS(I) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL - (ONE TO FIVE)	0	0	0	0	15	15
	0.01	0	1	3	7	11
	0.1	2	1	0	6	9
	0.5	1	0	2	3	6
	2.0	0	1	1	8	10

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATE WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

t LINEAR TREND BY MANTEL-HAENSZEL EXTENSION OF COCHRAN-ARMITAGE TEST (PETO), α=0.05.

M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
LIVER (CONTINUED)						
FOCUS(I) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL - (SIX TO FIFTEEN):	0	1	1	0	9	11
	0.01	1	0	0	13	14
	0.1	3	0	0	14	17
	0.5	2	1	2	14	19
	2.0	2	3	9	9	23
FOCUS(I) OF ALTERED CELLS, HEPATOCELLULAR, MULTIFOCAL - (SIXTEEN OR MORE):	0	0	0	2	25	27
	0.01	0	0	1	27	28
	0.1	1	0	1	24	26
	0.5	0	0	5	26	31
	2.0	1	1	8	12	22
TOTAL RATS WITH ONE OR MORE FOCI OF ALTERED CELLS:	0	1	1	2	49	53
	0.01	1	1	4	47	53
	0.1	6	1	1	44	52
	0.5	3	1	9	43	56
	2.0	3	5	18	29	55M
GRANULOMA(S) - MICRO, MULTIFOCAL:	0	0	0	0	3	3
	0.01	0	0	0	4	4
	0.1	1	0	0	1	2
	0.5	0	0	0	4	4
	2.0	0	0	3	2	5
HYPERPLASIA, BILE DUCTS, MULTIFOCAL - VERY SLIGHT:	0	0	0	2	28	30
	0.01	0	1	2	22	25
	0.1	3	0	0	19	22
	0.5	0	0	3	21	24
	2.0	1	0	5	9	15
HYPERPLASIA, BILE DUCTS, MULTIFOCAL - SLIGHT:	0	0	0	1	16	17
	0.01	1	0	5	10	16
	0.1	0	1	0	12	13
	0.5	1	0	1	10	12
	2.0	0	1	3	8	12
HYPERPLASIA, BILE DUCTS, MULTIFOCAL -	0	0	0	0	1	1[b]
	0.01	0	0	0	3	3
	0.1	0	0	0	2	2
	0.5	0	0	1	1	2
	2.0	0	0	1	0	1
TOTAL RATS WITH BILIARY HYPERPLASIA OF ANY DEGREE:	0	0	0	3	45	48
	0.01	1	1	7	35	44
	0.1	3	1	0	33	37
	0.5	1	0	5	32	38
	2.0	1	1	9	17	28*M

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANLAYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0.05.

M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
LIVER (CONTINUED)						
HYPERPLASIA - RETICULOENDOTHELIAL CELLS - MODERATE:	0	1	0	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
IMPACTION WITH OR WITHOUT CELLULAR DEBRIS OR WITH OR WITHOUT INFLAMMATION, EXTRAHEPATIC BILE DUCTS, FOCAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, PERIPORTAL, MULTIFOCAL - VERY SLIGHT:	0	0	0	0	15	15
	0.01	1	1	0	19	21
	0.1	1	1	0	13	15
	0.5	0	1	0	17	18
	2.0	1	1	4	13	19
INFLAMMATION - CHRONIC, PERIPORTAL, MULTIFOCAL - SLIGHT:	0	0	0	1	20	21
	0.01	0	0	2	6	8
	0.1	0	0	0	10	10
	0.5	0	0	1	9	10
	2.0	0	1	3	8	12
INFLAMMATION - CHRONIC, PERIPORTAL, MULTIFOCAL - MODERATE:	0	0	0	1	0	1[b]
	0.01	0	0	0	0	0*M
	0.1	0	0	0	2	2
	0.5	0	0	0	2	2
	2.0	0	0	0	0	0
TOTAL RATS WITH INFLAMMATION - CHRONIC, PERIPORTAL - ANY DEGREE:	0	0	0	2	35	37
	0.01	1	1	2	25	29
	0.1	1	1	0	25	27
	0.5	0	1	1	28	30
	2.0	1	2	7	21	31
NECROSIS, CENTRILOBULAR - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	1	0	0	0	1
	2.0	2	0	0	0	2
NECROSIS, CENTRILOBULAR - MODERATE:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANLAYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, $\alpha=0.05$.

M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), $\alpha=0.05$.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
LIVER (CONTINUED)						
NECROSIS, CENTRILOBULAR - SEVERE:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	1	0	1	0	2
	0.5	0	0	1	0	1
	2.0	0	0	1	1	2
VACUOLIZATION, PERIPORTAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
VACUOLIZATION CONSISTENT WITH FATTY CHANGE, HEPATOCELLULAR - SLIGHT:	0	0	0	0	4	4
	0.01	0	0	2	4	6
	0.1	0	0	0	2	2
	0.5	0	1	1	4	6
	2.0	0	2	1	3	6
VACUOLIZATION CONSISTENT WITH FATTY CHANGE, HEPATOCELLULAR - MODERATE:	0	0	0	2	0	2
	0.01	0	1	0	1	2
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
VACUOLIZATION CONSISTENT WITH FATTY CHANGE, HEPATOCELLULAR, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
THROMBUS - CHRONIC OR ORGANIZED:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	1	1	2
NECROSIS WITH ACCOMPANYING INFLAMMATION, FOCAL OR MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	2	1	3
	0.1	0	0	0	1	1
	0.5	2	0	1	3	6
	2.0	0	2	2	2	6
NECROSIS WITH ACCOMPANYING INFLAMMATION, MULTIFOCAL - MODERATE:	0	0	0	1	0	1[b]T
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, $\alpha=0.05$.

T LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, $\alpha=0.05$.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
HEART						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	0	4	32	38
	0.01	2	2	3	30	37
	0.1	8	1	2	29	40
	0.5	4	1	9	26	40
	2.0	4	3	13	16	36
DEGENERATION WITH OR WITHOUT INFLAMMATION, MYOCARDIUM, MULTIFOCAL - SLIGHT:	0	0	2	1	16	19
	0.01	0	0	5	16	21
	0.1	0	0	1	17	18
	0.5	0	0	1	16	17
	2.0	0	3	7	11	21
FIBROSIS, A/V VALVE, LEFT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
PIGMENT-LADEN MACROPHAGES, PAPILLARY MUSCLE, FOCAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
THRUMBUS - CHRONIC OR ORGANIZED, ATRIUM:	0	0	0	2	0	2
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	1	0	1
	2.0	0	0	1	0	1
DEGENERATION AND FIBROSIS, MYOCARDIUM, FOCAL - MODERATE:	0	0	0	0	2	2
	0.01	0	0	1	2	3
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	2	2
THROMBOEMBOLISM, VENTRICULAR LUMEN, RIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
SPLEEN						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	11	43	59
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	0	1	3	35	39
	0.01	1	1	3	38	43
	0.1	2	0	0	39	41
	0.5	1	1	6	36	44
	2.0	1	2	9	16	28
LEUKEMIA - FISCHER RAT, MALIGNANT, PRIMARY, METASTASIS, MULTIPLE ORGANS:	0	1	1	2	8	12
	0.01	1	1	3	6	11
	0.1	1	1	2	6	10
	0.5	0	0	2	5	7
	2.0	0	1	6	6	13
AMYLOID:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CHRONIC PASSIVE CONGESTION:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
FIBROSIS, FOCAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
VACUOLIZATION CONSISTENT WITH FATTY CHANGE, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
EXTRAMEDULLARY HEMATOPOIESIS--INCREASED - SLIGHT:	0	0	0	0	4	4
	0.01	0	0	1	2	3
	0.1	1	0	1	1	3
	0.5	0	0	1	0	1
	2.0	0	0	3	1	4

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
SPLEEN (CONTINUED)						
EXTRAMEDULLARY HEMATOPOIESIS--INCREASED - MODERATE:	0	0	0	1	2	3
	0.01	0	0	1	1	2
	0.1	2	0	0	1	3
	0.5	1	0	0	2	3
	2.0	2	1	2	4	9
EXTRAMEDULLARY HEMATOPOIESIS--INCREASED - SEVERE:	0	1	0	0	0	1T
	0.01	0	0	0	1	1
	0.1	2	0	1	0	3
	0.5	2	0	1	0	3
	2.0	1	2	1	1	5
TOTAL RATS WITH EXTRAMEDULLARY HEMATOPOIESIS--INCREASED - ANY DEGREE:	0	1	0	1	6	8T
	0.01	0	0	2	4	6
	0.1	5	0	2	2	9
	0.5	3	0	2	2	7
	2.0	3	3	6	6	18
PITUITARY						
NUMBER OF TISSUES EXAMINED	0	2	2	6	49	59
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	0	2	13	17
	0.01	1	2	2	8	13
	0.1	3	0	0	13	16
	0.5	3	0	5	9	17
	2.0	3	2	3	4	12
ADENOCARCINOMA, ANTERIOR (PARS DISTALIS), MALIGNANT, PRIMARY, NO METASTASIS:	0	0	1	2	4	7
	0.01	0	0	1	8	9
	0.1	1	0	0	0	1
	0.5	0	0	2	4	6
	2.0	0	1	1	3	5
ADENOMA, ANTERIOR (PARS DISTALIS), BENIGN, PRIMARY:	0	0	1	0	24	25
	0.01	1	0	3	26	30
	0.1	2	1	2	27	32
	0.5	0	1	3	23	27
	2.0	0	1	14	17	32M
CYST, ANTERIOR (PARS DISTALIS), FOCAL OR MULTIFOCAL:	0	0	0	0	4	4
	0.01	0	0	1	1	2
	0.1	0	0	0	4	4
	0.5	0	0	0	2	2
	2.0	1	1	0	1	3

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), α=0.05.
T LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, α=0.05

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
PITUITARY (CONTINUED)						
DILATED, SINUSOIDS:	0	0	0	0	3	3
	0.01	0	0	1	3	4
	0.1	1	0	0	1	2
	0.5	1	0	0	5	6
	2.0	0	1	3	1	5
HYPERPLASIA, ANTERIOR (PARS DISTALIS), FOCAL:	0	0	0	2	1	3
	0.01	0	0	0	3	3
	0.1	1	0	2	2	5
	0.5	0	0	2	1	3
	2.0	0	0	0	3	3
PIGMENT-LADEN MACROPHAGES, ANTERIOR (PARS DISTALIS), FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
PANCREAS						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	3	47	59
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	1	3	28	34
	0.01	2	2	6	30	40
	0.1	7	1	3	30	41
	0.5	3	1	10	31	45
	2.0	4	5	12	21	42
ADENOMA, ISLETS, BENIGN, PRIMARY:	0	0	0	0	2	2
	0.01	0	0	1	2	3
	0.1	0	0	0	3	3
	0.5	0	0	0	1	1
	2.0	0	0	1	0	1
ATROPHY, ACINI, FOCAL OR MULTIFOCAL - SLIGHT:	0	0	1	2	17	20
	0.01	0	0	2	12	14
	0.1	1	0	0	14	15
	0.5	1	0	2	10	13
	2.0	0	1	6	4	11
ATROPHY, ACINI, FOCAL OR MULTIFOCAL - MODERATE:	0	0	0	1	1	2[b]
	0.01	0	0	0	3	3
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	0	0	2	3	5

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
PANCREAS (CONTINUED)						
ATROPHY, ACINI, DIFFUSE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
DILATATION, DUCTS, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
HYPERPLASIA, ISLETS, FOCAL:	0	0	0	0	2	2
	0.01	0	0	0	2	2
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
BONE						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	6	49	59
	0.01	2	2	8	48	60
	0.1	8	1	4	44	57
	0.5	4	1	12	43	60
	2.0	4	7	20	29	60
OSTEOCHONDROMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
OSTEOPETROSIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
BONE MARROW						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
BONE MARROW (CONTINUED)						
WITHIN NORMAL LIMITS:	0	1	2	6	46	55
	0.01	2	2	7	44	55
	0.1	7	1	4	45	57
	0.5	2	1	10	40	53
	2.0	4	6	18	24	52
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
HYPERPLASIA, MYELOID:	0	1	0	0	3	4
	0.01	0	0	1	2	3
	0.1	1	0	0	1	2
	0.5	2	0	2	1	5
	2.0	0	1	3	4	8
HYPERPLASIA - RETICULOENDOTHELIAL CELLS, DIFFUSE - SEVERE:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
ADRENAL						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	3	14	21
	0.01	1	0	2	12	15
	0.1	6	0	3	16	25
	0.5	2	1	5	9	17
	2.0	4	4	8	8	24
ADENOMA, CORTEX, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
PHEOCHROMOCYTOMA, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	1	0	3	4
	0.1	0	0	0	2	2
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
ADRENAL (CONTINUED)						
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, MEDULLA, MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, CORTEX, MULTIFOCAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	1	1	2
DILATED, SINUSOIDS, FOCAL OR MULTIFOCAL:	0	0	0	0	3	3
	0.01	0	1	1	3	5
	0.1	0	0	0	2	2
	0.5	0	0	0	4	4
	2.0	0	1	3	0	4
FOCUS(I) OF ALTERED CELLS, CORTEX, FOCAL:	0	0	0	1	20	21
	0.01	1	0	3	18	22
	0.1	1	1	0	17	19
	0.5	1	0	4	14	19
	2.0	0	1	7	7	15
FOCUS(I) OF ALTERED CELLS, CORTEX, MULTIFOCAL:	0	0	0	0	13	13t
	0.01	0	0	1	14	15
	0.1	0	0	1	10	11
	0.5	0	0	0	16	16
	2.0	0	2	4	13	19
TOTAL RATS WITH FOCUS(I) OF ALTERED CELLS, CORTEX, FOCAL OR MULTIFOCAL:	0	0	0	1	33	34
	0.01	1	0	4	32	37
	0.1	1	1	1	27	30
	0.5	1	0	4	30	35
	2.0	0	3	11	20	34
HYPERPLASIA, MEDULLA, UNILATERAL:	0	0	0	1	3	4
	0.01	0	0	1	2	3
	0.1	0	0	0	1	1
	0.5	0	0	1	4	5
	2.0	0	0	1	1	2
MINERALIZATION, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
VACUOLIZATION CONSISTENT WITH FATTY CHANGE, CORTEX, BILATERAL - MODERATE:	0	0	0	2	0	2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
t LINEAR TREND BY MANTEL-HAENSZEL EXTENSION OF COCHRAN-ARMITAGE TEST (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
ADRENAL (CONTINUED)						
NECROSIS WITH ACCOMPANYING INFLAMMATION, CORTEX, FOCAL OR MULTIFOCAL:	0	0	0	1	0	1
	0.01	0	0	2	0	2
	0.1	1	0	0	0	1
	0.5	1	0	1	0	2
	2.0	0	0	0	0	0
KIDNEY						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	1	0	2	0	3
	0.01	1	0	0	2	3
	0.1	4	0	2	2	8
	0.5	3	0	1	1	5
	2.0	1	1	5	1	8
UNDIFFERENTIATED SARCOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, INTERSTITIUM, MULTIFOCAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	1	0	1	3
CAST(S), TUBULE(S), MULTIFOCAL - VERY SLIGHT:	0	0	0	0	7	7
	0.01	0	2	2	9	13
	0.1	0	0	1	7	8
	0.5	1	0	4	9	14
	2.0	0	2	1	4	7
CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY, BILATERAL - VERY SLIGHT:	0	0	1	3	30	34
	0.01	1	0	4	20	25
	0.1	1	1	0	22	24
	0.5	0	1	1	18	20
	2.0	0	2	12	14	28
CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY, BILATERAL - SLIGHT:	0	1	1	1	8	11
	0.01	0	0	0	11	11
	0.1	2	0	0	13	15
	0.5	0	0	2	15	17
	2.0	0	1	2	5	8

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
KIDNEY (CONTINUED)						
CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY, BILATERAL - MODERATE:	0	0	0	0	3	3
	0.01	0	0	2	4	6
	0.1	1	0	1	3	5
	0.5	0	0	2	0	2
	2.0	0	0	0	1	1
CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY, BILATERAL - SEVERE:	0	0	0	0	1	1[b]
	0.01	0	0	0	2	2
	0.1	0	0	0	0	0
	0.5	0	0	2	0	2
	2.0	0	0	1	1	2
TOTAL RATS WITH CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY - ANY DEGREE:	0	1	2	4	42	49T
	0.01	1	0	6	37	44
	0.1	4	1	1	38	44
	0.5	0	1	7	33	41
	2.0	0	3	15	21	39
MINERALIZATION, TUBULE(S), MULTIFOCAL - VERY SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
PIGMENT - HEMATOGENOUS - INCREASED, TUBULE(S):	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
HYDRONEPHROSIS AND DEGENERATION, UNILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
HYDRONEPHROSIS, BILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
PYELONEPHRITIS, UNILATERAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

[b] BECAUSE OF LOW INCIDENCE, THESE DATA WERE POOLED WITH DATA FROM NEXT LOWER SEVERITY FOR ANALYSIS. THE INDICATED SIGNIFICANCE IS FOR THE COMBINED VALUES RATHER THAN THE VALUE SHOWN.

T LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, $\alpha=0.05$.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
STOMACH						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	2	49	55
	0.01	2	1	7	45	55
	0.1	8	1	3	43	55
	0.5	4	1	6	41	52
	2.0	3	6	15	28	52
SQUAMOUS PAPILLOMA, NONGLANDULAR MUCOSA, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ECTOPIC TISSUE, GLANDULAR MUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
EDEMA, GLANDULAR SUBMUCOSA:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
EDEMA, NONGLANDULAR SUBMUCOSA:	0	0	0	1	0	1
	0.01	0	1	0	2	3
	0.1	0	0	1	0	1
	0.5	0	0	0	1	1
	2.0	0	1	2	0	3
EROSION, GLANDULAR MUCOSA, FOCAL OR MULTIFOCAL:	0	0	0	2	0	2
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	2	0	2
	2.0	1	0	1	0	2
HYPERKERATOSIS, NONGLANDULAR MUCOSA, DIFFUSE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
STOMACH (CONTINUED)						
HYPERPLASIA - EPITHELIAL, NONGLANDULAR MUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	1	0	1
	2.0	0	0	1	0	1
INFLAMMATION - CHRONIC, SUBMUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
ULCER, GLANDULAR MUCOSA, FOCAL OR MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	2	0	2
	2.0	0	0	1	0	1
ULCER, NONGLANDULAR MUCOSA, FOCAL OR MULTIFOCAL:	0	0	0	1	0	1
	0.01	0	1	1	0	2
	0.1	0	0	0	0	0
	0.5	0	0	4	0	4
	2.0	0	0	1	0	1
SMALL INTESTINE						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	6	50	60
	0.01	2	2	7	48	59
	0.1	8	1	4	46	59
	0.5	4	1	11	42	58
	2.0	4	7	20	29	60
MUCINOUS ADENOCARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
LEIOMYOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
SMALL INTESTINE (CONTINUED)						
INFLAMMATION - SUPPURATIVE, SUBMUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
ULCER, DUODENAL MUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
ECTOPIC PANCREAS, SUBMUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
CECUM						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	5	50	59
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	11	43	59
	2.0	4	7	20	28	59
PAPILLARY ADENOCARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
EDEMA, SUBMUCOSA:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
ULCER, MUCOSA, FOCAL:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	1	0	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
LARGE INTESTINE						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	1	2	6	45	54
	0.01	1	2	6	43	52
	0.1	5	1	4	40	50
	0.5	3	1	8	36	48
	2.0	2	6	16	24	48
EDEMA, SUBMUCOSA:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	2	0	2
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, MUSCULARIS - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
PARASITES - NEMATODE, LUMEN:	0	1	0	0	5	6T
	0.01	1	0	2	5	8
	0.1	3	0	0	7	10
	0.5	1	0	2	7	10
	2.0	2	1	5	5	13
CERVICAL LYMPH NODE						
NUMBER OF TISSUES EXAMINED	0	1	0	0	10	11
	0.01	0	2	1	18	21
	0.1	5	1	1	14	21
	0.5	3	0	2	11	16
	2.0	3	3	4	6	16
WITHIN NORMAL LIMITS:	0	1	0	0	5	6
	0.01	0	0	1	7	8
	0.1	2	0	1	5	8
	0.5	2	0	0	5	7
	2.0	3	1	2	4	10
PARAFOLLICULAR CELL ADENOCARCINOMA, (THYROID), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	1	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
T LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
CERVICAL LYMPH NODE (CONTINUED)						
INFLAMMATION - SUPPURATIVE, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
PLASMACYTOSIS OF MEDULLARY CORDS:	0	0	0	0	5	5
	0.01	0	1	0	11	12
	0.1	3	1	0	9	13
	0.5	1	0	1	6	8
	2.0	0	2	1	2	5
SINUS HISTIOCYTOSIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	1	0	2
	2.0	0	0	0	0	0
MEDIASTINAL LYMPH NODE						
NUMBER OF TISSUES EXAMINED	0	2	2	5	50	59
	0.01	2	2	8	46	58
	0.1	8	1	3	43	55
	0.5	4	1	11	40	56
	2.0	3	6	21	28	58
WITHIN NORMAL LIMITS:	0	2	2	5	50	59
	0.01	2	2	8	45	57
	0.1	8	1	3	43	55
	0.5	4	1	10	39	54
	2.0	3	6	21	26	56
UNDIFFERENTIATED CARCINOMA, (NASAL TURBINATES), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
HYPERPLASIA - REACTIVE, LYMPHOID:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
MEDIASTINAL LYMPH NODE (CONTINUED)						
SINUS HISTIOCYTOSIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
MESENTERIC LYMPH NODE						
NUMBER OF TISSUES EXAMINED	0	2	2	6	48	58
	0.01	2	2	8	48	60
	0.1	8	1	3	47	59
	0.5	4	1	11	43	59
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	6	48	58
	0.01	2	2	7	47	58
	0.1	8	1	3	47	59
	0.5	4	1	11	43	59
	2.0	4	6	16	27	53
ADENOCARCINOMA, (UTERUS), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
UNDIFFERENTIATED CARCINOMA, (NASAL TURBINATES), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
SINUS HISTIOCYTOSIS:	0	0	0	0	0	0
	0.01	0	0	1	1	2
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	5	0	6*
OTHER MISCELLANEOUS LYMPH NODES						
NUMBER OF TISSUES EXAMINED	0	0	0	0	1	1
	0.01	0	0	0	2	2
	0.1	0	0	0	0	0
	0.5	1	0	0	1	2
	2.0	0	0	2	3	5
ADENOCARCINOMA, (UTERUS), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, $\alpha=0.05$.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
OTHER MISCELLANEOUS LYMPH NODES (CONTINUED)						
HYPERPLASIA - REACTIVE, LYMPHOID, LUMBAR:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
HYPERPLASIA - REACTIVE, LYMPHOID, SUBCUTANEOUS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
INFLAMMATION - SUPPURATIVE, RENAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	0	0	1
	2.0	0	0	0	0	0
PLASMACYTOSIS OF MEDULLARY CORDS, RENAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	0	0	1
	2.0	0	0	0	0	0
PLASMACYTOSIS OF MEDULLARY CORDS, SUBCUTANEOUS:	0	0	0	0	1	1
	0.01	0	0	0	2	2
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	2	2
URINARY BLADDER						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	42	59
	2.0	4	6	21	28	59
WITHIN NORMAL LIMITS:	0	2	2	6	50	60
	0.01	2	2	7	46	57
	0.1	8	1	4	47	60
	0.5	4	1	11	42	58
	2.0	3	5	21	27	56
PAPILLOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	1	2

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
URINARY BLADDER (CONTINUED)						
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, SUBMUCOSA, MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CALCULUS(I), LUMEN:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
HYPERPLASIA, MUCOSA, DIFFUSE - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	0	0	1
HYPERPLASIA, MUCOSA, DIFFUSE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, DIFFUSE - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	1	0	0	0	1
OVARY						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	42	59
	2.0	4	7	21	28	60
WITHIN NORMAL LIMITS:	0	1	2	5	42	50
	0.01	2	2	7	42	53
	0.1	7	1	3	36	47
	0.5	4	1	10	32	47
	2.0	3	6	17	24	50
GRANULOSA - THECAL CELL TUMOR, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
OVARY (CONTINUED)						
LEIOMYOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
CYST, FOLLICLE(S), FOCAL:	0	0	0	0	2	2
	0.01	0	0	0	2	2
	0.1	1	0	1	3	5
	0.5	0	0	2	5	7M
	2.0	1	1	3	1	6
DISTENDED, OVARIAN BURSA, UNILATERAL:	0	1	0	1	3	5
	0.01	0	0	1	3	4
	0.1	0	0	0	6	6
	0.5	0	0	0	2	2
	2.0	0	0	0	2	2
HYPERPLASIA - ADENOMATOUS, RETE OVARII, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, UNILATERAL:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	2	2
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, BILATERAL:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	1	0	0	1	2
	0.5	0	0	0	2	2
	2.0	0	0	0	1	1
OVIDUCT						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	42	59
	2.0	4	7	21	28	60
WITHIN NORMAL LIMITS:	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	42	59
	2.0	4	7	21	28	60

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
UTERUS						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	42	59
	2.0	4	7	21	28	60
WITHIN NORMAL LIMITS:	0	2	2	5	16	25
	0.01	1	0	5	15	21
	0.1	5	0	3	18	26
	0.5	2	1	5	21	29
	2.0	3	4	10	8	25
ADENOCARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	2	2
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	1	2	3
ADENOCARCINOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	2	2
TOTAL RATS WITH AN ADENOCARCINOMA, MALIGNANT, PRIMARY, METASTASIC OR NON-METASTATIC:	0	0	0	0	1	1
	0.01	0	0	0	2	2
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	1	4	5M
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	5	5
	0.01	0	0	0	2	2
	0.1	0	0	0	1	1
	0.5	0	0	0	2	2
	2.0	1	0	1	1	3
ENDOMETRIAL STROMAL POLYP, BENIGN, PRIMARY:	0	0	0	0	17	17
	0.01	1	2	0	13	16
	0.1	1	1	1	15	18
	0.5	1	0	3	5	9
	2.0	0	1	4	9	14
ENDOMETRIAL STROMAL POLYP, BENIGN, PRIMARY, (TWO):	0	0	0	0	5	5
	0.01	0	0	0	5	5
	0.1	0	0	0	1	1
	0.5	0	0	2	3	5
	2.0	0	1	1	1	3

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
UTERUS (CONTINUED)						
ENDOMETRIAL STROMAL POLYP, BENIGN, PRIMARY, (FOUR):	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
TOTAL RATS WITH ONE OR MORE ENDOMETRIAL STROMAL POLYPS:	0	0	0	0	22	22
	0.01	1	2	0	18	21
	0.1	1	1	1	16	19
	0.5	1	0	5	8	14
	2.0	0	2	5	11	18
LEIOMYOSARCOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
STROMAL CELL SARCOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	1	0	0	1	2
	2.0	0	1	0	0	1
DILATATION, ENDOMETRIAL GLANDS:	0	0	0	1	10	11
	0.01	0	0	3	14	17
	0.1	1	0	0	13	14
	0.5	0	0	3	11	14
	2.0	0	0	5	7	12
HYPERPLASIA, ENDOMETRIAL GLANDS, FOCAL:	0	0	0	0	4	4
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
HYPERPLASIA - ADENOMATOUS, ENDOMETRIAL GLANDS, FOCAL:	0	0	0	0	1	1
	0.01	0	0	1	2	3
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	1	1	1	3
INFLAMMATION - CHRONIC ACTIVE, DIFFUSE - SLIGHT OR MODERATE:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	3	3
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
UTERUS (CONTINUED)						
INFLAMMATION - CHRONIC ACTIVE, DIFFUSE - SEVERE:	0	0	0	0	2	2
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
INFLAMMATION - SUPPURATIVE, DIFFUSE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, SUBMUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INTUSSUSCEPTION, UNILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	0	0	1
	2.0	0	0	0	0	0
THROMBUS - CHRONIC OR ORGANIZED, MUSCULARIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
CERVIX						
NUMBER OF TISSUES EXAMINED	0	2	2	6	49	59
	0.01	2	2	8	48	60
	0.1	8	1	4	46	59
	0.5	4	1	12	41	58
	2.0	4	7	21	27	59
WITHIN NORMAL LIMITS:	0	2	2	6	46	56
	0.01	2	2	6	46	56
	0.1	6	1	4	45	56
	0.5	3	1	11	40	55
	2.0	4	7	19	23	53
SQUAMOUS PAPILLOMA, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
CERVIX (CONTINUED)						
STROMAL CELL SARCOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	1	1	2
	0.1	2	0	0	0	2
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
ADENOCARCINOMA, (UTERUS), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
HYPERPLASIA - EPITHELIAL, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
HYPERTROPHY, MUSCULARIS:	0	0	0	0	1	1
	0.01	0	0	1	1	2
	0.1	0	0	0	1	1
	0.5	1	0	1	0	2
	2.0	0	0	0	2	2
ULCER, MUCOSA, MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CYST(S) WITH KERATINOUS DEBRIS, SUBMUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
INFLAMMATION - SUBACUTE TO CHRONIC, DIFFUSE - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
VAGINA						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	42	59
	2.0	4	7	19	28	58

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
VAGINA (CONTINUED)						
WITHIN NORMAL LIMITS:	0	2	2	5	45	54
	0.01	1	2	5	46	54
	0.1	5	1	4	43	53
	0.5	3	1	11	40	55
	2.0	4	6	15	25	50
LEIOMYOMA, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
LEIOMYOSARCOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	0	0	1
	2.0	0	0	0	0	0
ULCER, MUCOSA, MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CYST(S) WITH KERATINOUS DEBRIS, SUBMUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
EXUDATE, LUMEN:	0	0	0	1	4	5
	0.01	1	0	2	2	5
	0.1	3	0	0	4	7
	0.5	0	0	1	1	2
	2.0	0	1	4	3	8
LUNGS						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	1	1	3	16	21
	0.01	1	1	6	15	23
	0.1	4	1	3	15	23
	0.5	2	0	6	13	21
	2.0	3	2	15	6	26

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
LUNGS (CONTINUED)						
ADENOMA, ALVEOLI, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	0	0	0	0
PARAFOLLICULAR CELL ADENOCARCINOMA, (THYROID), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	1	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
UNDIFFERENTIATED CARCINOMA, (NASAL TURBINATES), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ADENOCARCINOMA, (UTERUS), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ALVEOLAR HISTIOCYTOSIS, FOCAL OR MULTIFOCAL - SLIGHT:	0	1	0	0	14	15t
	0.01	0	0	0	8	8
	0.1	0	0	0	15	15
	0.5	0	0	4	11	15
	2.0	1	1	1	13	16
CHRONIC PASSIVE CONGESTIVE CHANGES:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	1	0	1
	2.0	0	0	1	0	1
HYPERPLASIA - ADENOMATOUS, ALVEOLI, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	1	0	0	3	4
	0.5	2	0	0	2	4
	2.0	0	0	1	0	1
INFLAMMATION - CHRONIC, INTERSTITIUM, MULTIFOCAL - SLIGHT:	0	1	1	0	20	22
	0.01	0	0	1	22	23
	0.1	3	0	0	16	19
	0.5	1	1	1	19	22
	2.0	0	3	2	11	16

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
t LINEAR TREND BY MANTEL-HAENSZEL EXTENSION OF COCHRAN-ARMITAGE TEST (PETO) α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
LUNGS (CONTINUED)						
INFLAMMATION - CHRONIC, PERIBRONCHIOLAR, DIFFUSE - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
THROMBUS - ACUTE OR RECENT, MULTIFOCAL:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUBACUTE TO CHRONIC, INTERSTITIUM, FOCAL OR MULTIFOCAL - SLIGHT:	0	0	0	2	5	7
	0.01	1	0	0	7	8
	0.1	2	0	1	4	7
	0.5	0	0	0	6	6
	2.0	0	0	2	3	5
SKELETAL MUSCLE						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	6	50	60
	0.01	2	2	8	45	57
	0.1	8	1	4	46	59
	0.5	4	1	12	39	56
	2.0	4	7	21	29	61
ATROPHY - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION WITH OR WITHOUT INFLAMMATION, MUSCLE FIBERS, FOCAL - VERY SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	4	4
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
SKELETAL MUSCLE (CONTINUED)						
INFLAMMATION - CHRONIC, MULTIFOCAL - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SALIVARY GLAND						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	47	59
	0.1	8	1	4	47	60
	0.5	4	1	12	42	59
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	2	6	49	59
	0.01	2	2	8	47	59
	0.1	8	1	4	46	59
	0.5	4	1	12	39	56
	2.0	4	6	21	27	58
ATROPHY, ACINI, FOCAL OR MULTIFOCAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	0	0	2	2
GRANULOMA(S) - MICRO, DUCTS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
THYMUS						
NUMBER OF TISSUES EXAMINED	0	2	2	4	47	55
	0.01	2	1	8	45	56
	0.1	8	1	4	45	58
	0.5	2	1	12	40	55
	2.0	3	5	21	28	57

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
THYMUS (CONTINUED)						
WITHIN NORMAL LIMITS:	0	2	2	4	45	53
	0.01	2	1	8	43	54
	0.1	8	0	4	42	54
	0.5	2	1	11	37	51
	2.0	3	5	20	24	52
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CYST:	0	0	0	0	1	1
	0.01	0	0	0	2	2
	0.1	0	1	0	3	4
	0.5	0	0	1	3	4
	2.0	0	0	1	4	5M
MEDIASTINAL TISSUE						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	2	5	48	57
	0.01	1	2	7	46	56
	0.1	8	1	4	45	58
	0.5	4	1	12	41	58
	2.0	4	6	20	28	58
INFLAMMATION - CHRONIC, MULTIFOCAL - SLIGHT:	0	0	0	1	2	3
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	1	1
INFLAMMATION - CHRONIC, MULTIFOCAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
PERIARTERITIS - MODERATE:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
MEDIASTINAL TISSUE (CONTINUED)						
THROMBUS - CHRONIC OR ORGANIZED, MULTIFOCAL:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
ECTOPIC PARATHYROID:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
AORTA						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
ESOPHAGUS						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	2	6	50	60
	0.01	2	2	8	47	59
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
INFLAMMATION - CHRONIC, DIFFUSE - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
THYROID GLAND						
NUMBER OF TISSUES EXAMINED	0	2	2	6	48	58
	0.01	2	2	8	47	59
	0.1	8	1	4	46	59
	0.5	3	1	12	42	58
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	2	5	32	41
	0.01	2	1	5	34	42
	0.1	7	1	3	30	41
	0.5	2	1	9	28	40
	2.0	3	4	15	15	37
ADENOCARCINOMA, FOLLICLE(S), MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	2	3
PAPILLARY ADENOMA, FOLLICLE(S), BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	1	2	3
TOTAL RATS WITH THYROID FOLLICULAR TUMOR, ADENOCARCINOMA OR PAPILLARY ADENOMA:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	0	2	3	5M
PARAFOLLICULAR CELL ADENOCARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
PARAFOLLICULAR CELL ADENOCARCINOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	1	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
PARAFOLLICULAR CELL ADENOMA, BENIGN, PRIMARY:	0	0	0	0	3	3
	0.01	0	0	1	6	7
	0.1	0	0	0	2	2
	0.5	0	0	1	4	5
	2.0	0	0	0	3	3
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, FOCAL - VERY SLIGHT:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
THYROID GLAND (CONTINUED)						
CYSTIC DILATATION, FOLLICLE(S), FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	1	1
	2.0	0	1	1	1	3
HYPERPLASIA, PARAFOLLICULAR CELLS, FOCAL:	0	0	0	1	5	6
	0.01	0	0	1	5	6
	0.1	0	0	1	6	7
	0.5	0	0	2	5	7
	2.0	1	2	3	4	10
HYPERPLASIA, PARAFOLLICULAR CELLS, MULTIFOCAL:	0	0	0	0	3	3
	0.01	0	0	0	0	0
	0.1	1	0	0	5	6
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
CYST(S) WITH KERATINOUS DEBRIS, FOCAL:	0	0	0	0	5	5
	0.01	0	1	0	3	4
	0.1	0	0	0	2	2
	0.5	1	0	0	4	5
	2.0	0	0	0	2	2
PARATHYROID GLAND						
NUMBER OF TISSUES EXAMINED	0	2	2	5	42	51
	0.01	1	2	8	38	49
	0.1	7	1	4	40	52
	0.5	3	1	12	40	56
	2.0	4	5	21	29	59
WITHIN NORMAL LIMITS:	0	2	2	5	42	51
	0.01	1	2	8	38	49
	0.1	7	1	4	40	52
	0.5	3	1	10	40	54
	2.0	4	5	21	29	59
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
HYPERPLASIA, BILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
TRACHEA						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
SKIN						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	20	29	60
WITHIN NORMAL LIMITS:	0	2	0	5	48	55
	0.01	1	2	7	46	56
	0.1	8	1	4	46	59
	0.5	4	1	11	41	57
	2.0	4	7	19	29	59
BASAL CELL ADENOMA, BENIGN, PRIMARY:	0	0	0	1	0	1
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
SQUAMOUS CELL CARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
SQUAMOUS PAPILLOMA, BENIGN, PRIMARY:	0	0	1	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
FIBROUS HISTIOCYTOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
SKIN (CONTINUED)						
EPIDERMAL INCLUSION CYST:	0	0	1	0	1	2
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	1	0	1
INFLAMMATION - CHRONIC ACTIVE, SUBCUTANEOUS, FOCAL - MODERATE:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, EPIDERMIS, MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
STRANGULATED OR NECROTIC FAT, FOCAL:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
MAMMARY GLAND						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	3	1	11	43	58
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	0	2	12	16
	0.01	1	1	2	10	14
	0.1	3	1	2	15	21
	0.5	2	0	2	11	15
	2.0	2	2	4	7	15
ADENOCARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	2	2Tt
	0.01	0	0	0	1	1
	0.1	0	0	0	1	1
	0.5	0	0	0	2	2
	2.0	0	2	3	1	6
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	1	2	3
	2.0	0	0	1	1	2

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
T LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, α=0.05.
t LINEAR TREND BY MANTEL-HAENSZEL EXTENSION OF COCHRAN-ARMITAGE TEST (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMIN SACRIF
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50
	0.01	2	2	8	48
	0.1	8	1	4	47
	0.5	4	1	12	43
	2.0	4	7	21	29
MAMMARY GLAND (CONTINUED)					
FIBROADENOMA, BENIGN, PRIMARY:	0	0	0	1	8
	0.01	0	0	1	9
	0.1	0	0	0	8
	0.5	0	1	3	10
	2.0	1	0	3	9
FIBROADENOMA, BENIGN, PRIMARY, (TWO):	0	0	0	0	1
	0.01	0	0	0	1
	0.1	0	0	0	1
	0.5	0	0	1	1
	2.0	0	1	0	1
FIBROADENOMA, BENIGN, PRIMARY, (THREE):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	0	0	0	1
FIBROADENOMA, BENIGN, PRIMARY, (FOUR):	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	1	0
	2.0	0	0	0	0
FIBROMA, BENIGN, PRIMARY:	0	0	0	0	0
	0.01	0	0	0	0
	0.1	0	0	0	0
	0.5	0	0	0	0
	2.0	1	0	3	1
TOTAL RATS WITH ONE OR MORE BENIGN TUMOR(S):	0	0	0	1	9
	0.01	0	0	1	10
	0.1	0	0	0	9
	0.5	0	1	5	13
	2.0	2	1	7	13
DILATATION, DUCTS:	0	0	1	2	26
	0.01	0	1	5	17
	0.1	1	0	1	22
	0.5	0	1	3	14
	2.0	0	2	6	8

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAEN (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
MAMMARY GLAND (CONTINUED)						
GALACTOCELE:	0	0	0	0	3	3
	0.01	0	0	1	1	2
	0.1	0	0	0	2	2
	0.5	0	0	0	3	3
	2.0	0	0	1	1	2
GALACTOCELE, (TWO):	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
HYPERPLASIA - EPITHELIAL, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC ACTIVE, FOCAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
INFLAMMATION - SUPPURATIVE, FOCAL - MODERATE:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
PIGMENT-LADEN MACROPHAGES, INTERSTITIUM, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
HYPERPLASIA OFTEN ACCOMPANIED BY DUCT ECTASIA:	0	0	1	2	8	11
	0.01	0	0	1	16	17
	0.1	4	0	1	6	11
	0.5	1	0	3	13	17
	2.0	0	2	6	10	18

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERM SACR
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	
	0.01	2	2	8	
	0.1	8	1	4	
	0.5	4	1	12	
	2.0	4	7	21	
CLITORAL GLAND					
NUMBER OF TISSUES EXAMINED	0	0	0	0	
	0.01	0	0	0	
	0.1	1	0	1	
	0.5	0	0	1	
	2.0	0	0	2	
ADENOCARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	
	0.01	0	0	0	
	0.1	0	0	0	
	0.5	0	0	1	
	2.0	0	0	0	
ADENOMA, BENIGN, PRIMARY:	0	0	0	0	
	0.01	0	0	0	
	0.1	1	0	1	
	0.5	0	0	0	
	2.0	0	0	2	
IMPACTION WITH OR WITHOUT CELLULAR DEBRIS OR WITH OR WITHOUT INFLAMMATION:	0	0	0	0	
	0.01	0	0	0	
	0.1	0	0	0	
	0.5	0	0	0	
	2.0	0	0	0	
INFLAMMATION - CHRONIC ACTIVE, UNILATERAL - SEVERE:	0	0	0	0	
	0.01	0	0	0	
	0.1	0	0	0	
	0.5	0	0	0	
	2.0	0	0	0	
EYE					
NUMBER OF TISSUES EXAMINED	0	2	2	6	
	0.01	2	2	8	
	0.1	8	1	4	
	0.5	4	1	12	
	2.0	4	6	21	
WITHIN NORMAL LIMITS:	0	2	2	6	
	0.01	1	2	8	
	0.1	8	1	3	
	0.5	4	1	11	
	2.0	3	6	19	
CATARACT, LENS, UNILATERAL:	0	0	0	0	
	0.01	0	0	0	
	0.1	0	0	0	
	0.5	0	0	0	
	2.0	0	0	0	

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST,
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-H (PETO) p=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
EYE (CONTINUED)						
INCREASED VASCULARITY, CORNEA, UNILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	1	0	1
	2.0	0	0	0	1	1
INFLAMMATION - CHRONIC, CHOROID, BILATERAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC OR CHRONIC ACTIVE, CORNEA, UNILATERAL - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	1	0	1
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
INFLAMMATION - SUBACUTE, CONJUNCTIVA, FOCAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
PHTHISIS BULBI, UNILATERAL:	0	0	0	0	1	1
	0.01	1	0	0	3	4
	0.1	0	0	0	2	2
	0.5	0	0	0	3	3
	2.0	1	0	1	1	3
PHTHISIS BULBI, BILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
ANTERIOR SYNECHIA, IRIS, UNILATERAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
TONGUE						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
TONGUE (CONTINUED)						
WITHIN NORMAL LIMITS:	0	2	1	6	39	48
	0.01	2	2	8	37	49
	0.1	8	1	3	37	49
	0.5	3	1	11	35	50
	2.0	4	7	19	24	54
SQUAMOUS PAPILLOMA, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	1	2
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, SUBMUCOSA - SLIGHT:	0	0	1	0	5	6T
	0.01	0	0	0	4	4
	0.1	0	0	1	4	5
	0.5	0	0	0	4	4
	2.0	0	0	0	1	1
ATROPHY, SUBMUCOSAL GLANDS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	3	3
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
GRANULOMA(S) - MICRO, SUBMUCOSAL GLANDS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
HYPERPLASIA - EPITHELIAL, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, PERINEURAL - SLIGHT:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	0	0	1	1
INFLAMMATION - CHRONIC OR CHRONIC ACTIVE, SUBMUCOSAL GLANDS - SLIGHT:	0	0	0	0	2	2
	0.01	0	0	0	2	2
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
T LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
TONGUE (CONTINUED)						
ULCER, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	0	0	1
	2.0	0	0	0	0	0
PERIARTERITIS - SLIGHT:	0	0	0	0	2	2
	0.01	0	0	0	3	3
	0.1	0	0	0	2	2
	0.5	0	0	1	2	3
	2.0	0	0	0	0	0
FOREIGN BODY REACTION, SUBMUCOSAL GLANDS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	1	1	2
ORAL TISSUES						
NUMBER OF TISSUES EXAMINED	0	1	0	0	8	9
	0.01	1	0	1	10	12
	0.1	0	1	0	14	15
	0.5	2	0	3	4	9
	2.0	0	1	7	7	15
SQUAMOUS CELL CARCINOMA, GINGIVA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
SQUAMOUS CELL CARCINOMA, HARD PALATE, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	1	0	1	0	2
	2.0	0	0	0	0	0
SQUAMOUS PAPILLOMA, HARD PALATE OR LIP, BENIGN, PRIMARY:	0	0	0	0	0	0
	0.01	0	0	0	3	3
	0.1	0	0	0	2	2
	0.5	0	0	0	1	1
	2.0	0	1	2	2	5*M
AMELOBLASTIC ODONTOMA, TOOTH, BENIGN, PRIMARY:	0	1	0	0	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, $\alpha=0.05$.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), $\alpha=0.05$.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
ORAL TISSUES (CONTINUED)						
ABSCESS, PERIDONTAL, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
HYPERPLASIA - EPITHELIAL, HARD PALATE, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	2	2
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	0	4	4
INFLAMMATION - CHRONIC ACTIVE, PERIDONTAL, FOCAL OR MULTIFOCAL:	0	0	0	0	0	0
	0.01	0	0	1	2	3
	0.1	0	0	0	1	1
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
INFLAMMATION - SUBACUTE, GINGIVA, MULTIFOCAL:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
NECROSIS, TOOTH:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	2	2
	0.5	0	0	1	1	2
	2.0	0	0	0	1	1
ULCER, MUCOSA, FOCAL - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
FOREIGN BODY REACTION, PERIDONTAL, FOCAL OR MULTIFOCAL:	0	0	0	0	7	7
	0.01	0	0	0	3	3
	0.1	0	1	0	8	9
	0.5	1	0	1	2	4
	2.0	0	0	2	1	3
DEVELOPMENTAL DEFECT, TOOTH:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
NASAL TISSUES						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	2	2	2	40	46
	0.01	1	2	7	34	44
	0.1	7	1	3	37	48
	0.5	4	1	6	34	45
	2.0	4	5	15	22	46
UNDIFFERENTIATED CARCINOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
CYSTIC DILATATION, SUBMUCOSAL GLANDS, FOCAL:	0	0	0	0	0	0
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
DEGENERATION, LATERAL NASAL GLANDS, FOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC ACTIVE, OLFACTORY EPITHELIUM, FOCAL - MODERATE:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC ACTIVE, RESPIRATORY EPITHELIUM, FOCAL OR MULTIFOCAL - SLIGHT OR MODERATE:	0	0	0	1	1	2
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	1	0	1	2
INFLAMMATION - SUPPURATIVE, RESPIRATORY EPITHELIUM, MULTIFOCAL - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
NASAL TURBINATES (CONTINUED)						
INFLAMMATION - SUPPURATIVE, NASOLACRIMAL DUCT, UNILATERAL:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	1	0	0	3	4
	0.5	0	0	1	1	2
	2.0	0	0	2	0	2
THROMBUS - ACUTE OR RECENT, MULTIFOCAL:	0	0	0	2	0	2
	0.01	1	0	0	0	1
	0.1	1	0	0	0	1
	0.5	0	0	2	0	2
	2.0	0	0	2	0	2
CYST(S) WITH KERATINOUS DEBRIS, NASOLACRIMAL DUCT, UNILATERAL OR BILATERAL:	0	0	0	2	2	4
	0.01	0	0	0	8	8
	0.1	0	0	0	6	6
	0.5	0	0	3	2	5
	2.0	0	1	1	4	6
FOREIGN BODY REACTION, FOCAL:	0	0	0	1	5	6
	0.01	0	0	1	6	7
	0.1	0	0	1	1	2
	0.5	0	0	0	3	3
	2.0	0	0	1	2	3
MESENTERIC TISSUE						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	3	47	59
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
WITHIN NORMAL LIMITS:	0	1	2	3	44	50
	0.01	2	2	5	42	51
	0.1	4	0	3	37	44
	0.5	1	1	5	37	44
	2.0	3	6	15	22	46
ADENOCARCINOMA, (UTERUS), MALIGNANT, SECONDARY:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1
ATROPHY, ADIPOSE TISSUE:	0	1	0	1	1	3
	0.01	0	0	2	2	4
	0.1	1	1	0	2	4
	0.5	3	0	5	0	8
	2.0	0	1	6	1	8

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
T LINEAR TREND BY THE COCHRAN-ARMITAGE TEST, α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
MESENTERIC TISSUE (CONTINUED)						
ECTOPIC SPLEEN:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	0	0	1	1	2
	2.0	0	0	0	0	0
INFLAMMATION - CHRONIC, MULTIFOCAL - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	1	1
	2.0	0	0	1	0	1
STRANGULATED OR NECROTIC FAT:	0	0	0	2	4	6
	0.01	0	0	1	3	4
	0.1	2	0	0	6	8
	0.5	0	0	0	4	4
	2.0	1	0	0	5	6
PERIARTERITIS - SLIGHT:	0	0	0	0	0	0
	0.01	0	0	0	2	2
	0.1	0	0	0	3	3
	0.5	0	0	1	0	1
	2.0	0	0	0	0	0
THROMBUS - CHRONIC OR ORGANIZED, BLOOD VESSELS, MULTIFOCAL - SEVERE:	0	0	0	1	0	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
LACRIMAL/HARDERIAN GLAND(S)						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	1	0	3	21	25
	0.01	2	0	6	23	31
	0.1	5	0	1	22	28
	0.5	1	1	6	17	25
	2.0	3	3	9	15	30
INFLAMMATION - CHRONIC, UNILATERAL:	0	1	2	3	19	25
	0.01	0	1	2	17	20
	0.1	3	1	3	15	22
	0.5	2	0	3	19	24
	2.0	1	2	10	8	21

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
LACRIMAL/HARDERIAN GLAND(S) (CONTINUED)						
INFLAMMATION - CHRONIC, BILATERAL:	0	0	0	0	8	8
	0.01	0	1	0	6	7
	0.1	0	0	0	9	9
	0.5	1	0	2	7	10
	2.0	0	1	2	6	9
DEGENERATION--SECONDARY TO ORBITAL BLEEDING, UNILATERAL:	0	0	0	0	2	2
	0.01	0	0	0	2	2
	0.1	0	0	0	2	2
	0.5	0	0	1	1	2
	2.0	0	0	0	2	2
LARYNX						
NUMBER OF TISSUES EXAMINED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	3	46	58
	0.5	4	1	12	42	59
	2.0	4	6	21	29	60
WITHIN NORMAL LIMITS:	0	2	2	4	39	47
	0.01	2	2	5	36	45
	0.1	7	1	1	36	45
	0.5	3	1	12	33	49
	2.0	4	6	19	27	-56
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, SUBMUCOSA, MULTIFOCAL - MODERATE:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	2	0	2
IMPACTION WITH OR WITHOUT CELLULAR DEBRIS OR WITH OR WITHOUT INFLAMMATION, SUBMUCOSAL GLANDS:	0	0	0	2	8	10
	0.01	0	0	1	9	10
	0.1	0	0	2	10	12
	0.5	1	0	0	7	8
	2.0	0	0	0	0	0*M
INFLAMMATION - SUPPURATIVE, DIFFUSE - MODERATE:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, SUBMUCOSAL GLANDS, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	2	2
	0.1	1	0	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.
* INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, FISHER'S EXACT PROBABILITY TEST, α=0.05.
M INDICATES A STATISTICAL DIFFERENCE FROM THE CONTROL GROUP, MORTALITY ADJUSTMENT VIA MANTEL-HAENSZEL PROCEDURE (PETO), α=0.05.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS	0	2	2	6	50	60
NECROPSIED DURING	0.01	2	2	8	48	60
THE TIME PERIOD	0.1	8	1	4	47	60
INDICATED	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
LARYNX (CONTINUED)						
ULCER, MUCOSA, FOCAL:	0	0	0	0	0	0
	0.01	0	0	1	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
FOREIGN BODY REACTION, FOCAL:	0	0	0	0	1	1
	0.01	0	0	0	1	1
	0.1	0	0	0	0	0
	0.5	0	0	0	2	2
	2.0	0	0	0	2	2
AUDITORY SEBACEOUS (ZYMBAL) GLAND(S)						
NUMBER OF TISSUES EXAMINED	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	1	0	2
WITHIN NORMAL LIMITS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
CARCINOMA, MALIGNANT, PRIMARY, NO METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	1	0	0	1
PERITONEUM						
NUMBER OF TISSUES EXAMINED	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
INFLAMMATION - CHRONIC, DIFFUSE - MODERATE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	1	0	0	0	1
INFLAMMATION - SUPPURATIVE, DIFFUSE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 24 (CONTINUED)

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Histopathologic Observations[a] - Females

	DOSE (MG/KG/DAY)	1-18 MONTHS	19-21 MONTHS	22 MONTHS TO TERMINATION	TERMINAL SACRIFICE	CUMULATIVE RESULTS
NUMBER OF FEMALE RATS NECROPSIED DURING THE TIME PERIOD INDICATED	0	2	2	6	50	60
	0.01	2	2	8	48	60
	0.1	8	1	4	47	60
	0.5	4	1	12	43	60
	2.0	4	7	21	29	61
PLEURA						
NUMBER OF TISSUES EXAMINED	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	1	0	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUBACUTE, MULTIFOCAL - MODERATE:	0	0	0	0	0	0
	0.01	1	0	0	0	1
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
INFLAMMATION - SUPPURATIVE, DIFFUSE - SEVERE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	1	0	0	0	1
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
MULTIPLE ORGANS						
NUMBER OF TISSUES EXAMINED	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	2	0	2
	2.0	0	0	2	1	3
HISTIOCYTIC SARCOMA, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	2	0	2
	2.0	0	0	1	0	1
LEUKEMIA - LYMPHOID CELL, MALIGNANT, PRIMARY, METASTASIS:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	1	0	1
HYPERPLASIA - REACTIVE, LYMPHOID:	0	0	0	0	1	1
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	0	0
MINERALIZATION--SECONDARY TO RENAL DISEASE:	0	0	0	0	0	0
	0.01	0	0	0	0	0
	0.1	0	0	0	0	0
	0.5	0	0	0	0	0
	2.0	0	0	0	1	1

[a] DATA PRESENTED ARE NUMBER OF RATS HAVING THE STATED OBSERVATION.

TABLE 25

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Summary of Tumor Incidence

SEX	MALES					FEMALES				
DOSE (MG/KG/DAY)	0	0.01	0.1	0.5	2.0	0	0.01	0.1	0.5	2.0
NUMBER EXAMINED MICROSCOPICALLY	60	60	60	60	60	60	60	60	60	61
TOTAL ANIMALS WITH PRIMARY TUMORS	58	59	60	60	58	52	57	53	57	59
TOTAL PRIMARY TUMORS	162	156	174	154	197	107	123	96	117	163
TOTAL ANIMALS WITH BENIGN TUMORS	58	58	60	58	58	45	52	49	51	52
TOTAL BENIGN TUMORS	128	127	142	117	147	83	94	79	90	113
TOTAL ANIMALS WITH MALIGNANT TUMORS	31	26	29	36	43	23	23	16	24	40
TOTAL MALIGNANT TUMORS	34	29	32	37	50	24	29	17	27	50

TABLE 26

ACRYLAMIDE: A TWO-YEAR DRINKING WATER CHRONIC TOXICITY-ONCOGENICITY STUDY IN FISCHER 344 RATS

Observations Suggestive of Tumors for Which No Final Diagnosis was Made

DOSE (mg/kg/day)	Animal Number	Disposition
Males		
0.1	80A3413	Islet cell tumor noted in pancreatic lymph node on histopathologic examination. No primary found in pancreas either at necropsy or extensive examination of all fixed tissue (including additional histopathology).
0.5	80A3493	One cm mass in right axilla described on palpable mass records 15 days prior to necropsy. Mass not noted at necropsy and upon extensive examination of fixed tissues.
Females		
0.01	80A3789	Small (0.2-0.5 cm) uterine polyp noted at necropsy. Histopathologically, an endometrial stromal polyp was not found; however, a slightly elevated focus of dilated endometrial glands was noted.
0.5	80A4013	A pale, soft polypoid mass less than 0.2 cm in size was noted at necropsy in the glandular mucosa of the stomach. This was not identified histologically (in spite of multiple sections).
2.0	80A4095	Large (2.6-5.0 cm, 6-20 gm) mottled soft mass involving left ovary. Reproductive tract misplaced after photography with no tissues present with the fixed tissues.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Ronald L. Keener, Ph.D.
Regulatory Affairs Director, Product Integrity Department
Rohm and Haas Company
Independence Mall West
Philadelphia, Pennsylvania 19105

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 0 6 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

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Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12113A

Triage of 8(e) Submissions

Date sent to triage: 12/8/95

NON-CAP CAP

Submission number: 12113A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX	CTOX w/neur.	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

~~THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE RE-FILE AFTER TRIAGE DATABASE ENTRY~~

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entire document: 0 (1) 2 **pages** 1 **pages** 1, tabs

Notes:

Contractor reviewer : LPS **Date:** 3/10/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # 8EHQ- 0992 -12113 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: Rohm and Haas Company

SUB. DATE: 08/24/92 OTS DATE: 09/03/92 CSRAD DATE: 02/01/95

CHEMICAL NAME: Acrylamide

CAS# 79-06-1

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

INFORMATION TYPE:		P	F	C
0201	ONCO (HUMAN)	01	02	04
(0202)	ONCO (ANIMAL)	01	(02)	04
0203	CELL TRANS (IN VITRO)	01	02	04
0204	MUTA (IN VITRO)	01	02	04
0205	MUTA (IN VIVO)	01	02	04
0206	REPRO/TERATO (HUMAN)	01	02	04
0207	REPRO/TERATO (ANIMAL)	01	02	04
0208	NEURO (HUMAN)	01	(02)	04
(0209)	NEURO (ANIMAL)	01	02	04
0210	ACUTE TOX. (HUMAN)	01	02	04
0211	CHR. TOX. (HUMAN)	01	02	04
0212	ACUTE TOX. (ANIMAL)	01	02	04
0213	SUB ACUTE TOX (ANIMAL)	01	02	04
0214	SUB CHRONIC TOX (ANIMAL)	01	02	04
(0215)	CHRONIC TOX (ANIMAL)	01	(02)	04

INFORMATION TYPE:		P	F	C
0216	EPI/CLIN	01	02	04
0217	HUMAN EXPOS (PROD CONTAM)	01	02	04
0218	HUMAN EXPOS (ACCIDENTAL)	01	02	04
0219	HUMAN EXPOS (MONITORING)	01	02	04
0220	ECO/AQUA TOX	01	02	04
0221	ENV. OCCC/REL/FATE	01	02	04
0222	EMER INCI OF ENV CONTAM	01	02	04
0223	RESPONSE REQEST DELAY	01	02	04
0224	PROD/COMP/CHEM ID	01	02	04
0225	REPORTING RATIONALE	01	02	04
0226	CONFIDENTIAL	01	02	04
0227	ALLERG (HUMAN)	01	02	04
0228	ALLERG (ANIMAL)	01	02	04
0239	METAB/PHARMACO (ANIMAL)	01	02	04
0240	METAB/PHARMACO (HUMAN)	01	02	04

INFORMATION TYPE:		P	F	C
0241	IMMUNO (ANIMAL)	01	02	04
0242	IMMUNO (HUMAN)	01	02	04
(0243)	CHEM/PHYS PROP	01	02	04
0244	CLASTO (IN VITRO)	01	02	04
0245	CLASTO (ANIMAL)	01	02	04
0246	CLASTO (HUMAN)	01	02	04
0247	DNA DAM/REPAIR	01	02	04
(0248)	PROD/USE/PROC	01	02	04
0251	MSDS	01	02	04
0299	OTHER			

TRIAGE DATA: NON-CBI INVENTORY
(YES)
CAS SR NO
IN TERMINI

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES: RAT

TOXICOLOGICAL CONCERN:
LOW
MED
[HIGH]

USE: Manuf. of polymers: copolymers for flocculating agents: viscosifiers

PRODUCTION: to deliver charged

COMMENTS: Rats (Fischer 344) were provided drinking waters formulated to deliver 0, 0.01, 0.1, 0.5 or 2 mg acrylamide/kg for 2 years. Degeneration of the peripheral (femoral and tibial) nerves were observed 2.0 mg/kg/day. Body weights were decreased in males given 0.5 mg/kg/day. The dermal mesothelioma was increased in males at 0.1 mg/kg/day. The NOAEL is: 0.01 mg/kg/day

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # 8EHQ- 0992 -12113 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: Rohm and Haas Company

SUB. DATE: 08/24/92 OTS DATE: 09/03/92 CSRAD DATE: 02/01/95

CHEMICAL NAME: Acrylamide

CAS# 79-06-1

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER PROTECTION
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
(0202)	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
(0209)	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
(0215)	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
(0248)	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	

TRIAGE DATA: NON-CBI INVENTORY
(YES)
CAS SR NO
[illegible]

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
[illegible]

SPECIES
RAT

TOXICOLOGICAL CONCERN:
LOW
MED
(HIGH)

USE: manuf. of polymers : copolymers for flocculating agents : viscosifiers

PRODUCTION:

12113a

H

Carcinogenicity of acrylamide in Fischer 344 rats is of high concern. Male and female rats (60/sex/dose) received drinking water at concentrations designed to provide 0, 0.01, 0.1, 0.5, or 2.0 mg acrylamide/kg/day for 2 years. An additional 10/sex/dose were sacrificed at 6, 12, and 18 months. At the high dose, mortality was increased and there was a biologically significant increase in tumors at several sites, primarily at the terminal sacrifice. In high-dose females, there was a significant increase in fibroadenomas and adenocarcinomas of the mammary gland; malignant central nervous system tumors, particularly astrocytomas; and tumors of the follicular epithelium of the thyroid gland (combined benign and malignant), mouth (benign), uterus (malignant), and clitoral gland (benign). In high-dose males, there was a biologically significant increase in scrotal mesothelioma (malignant) and follicular epithelium of the thyroid gland (benign). In addition, male rats at the high dose had an increased incidence of central nervous system tumors when compared to historical controls, but not when compared to concurrent controls. Scrotal mesothelioma also showed a dose-related increase, with significantly increased incidence at 0.5 mg/kg/day, and an increase that did not reach statistical significance at 0.1 mg/kg/day. Benign tumors of the mammary gland and clitoral gland showed a nonsignificant increase indicative of a dose-response trend at 0.5 mg/kg/day. There were no other significant effects on tumor incidence at 0.5 mg/kg/day or less. The only significant noncancer effect was degeneration of the peripheral nerves at the high dose; there was no effect on hematology, clinical chemistry, or urinalysis parameters.